A Smorgasbord of Exceedingly Unusual Behaviours

A talk by Nick Crawford

Introducing

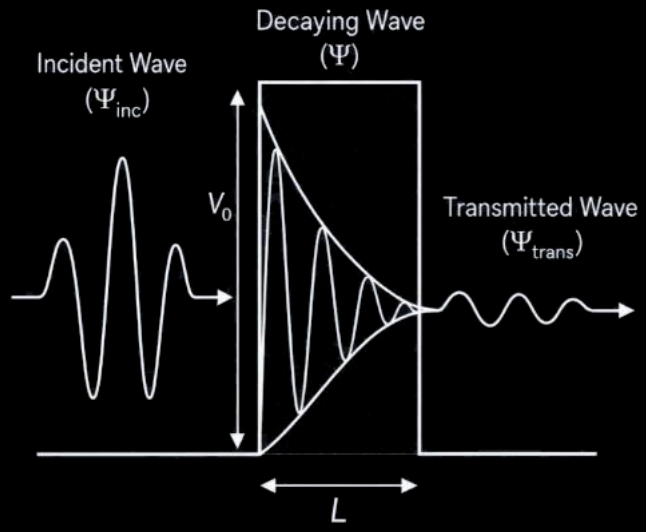
The Metabolic Approach to Cancer

The Quantum Tunnelling Effect

Quantum tunneling is the phenomenon where a particle passes through a potential barrier that it classically could not surmount.



George Gamow
(1904–1968)
Pioneer who first explained quantum tunneling in alpha decay.



$$T \approx e^{-2kL}$$

T = Transmission Probability
L = Barrier Width
k = Decay Constant

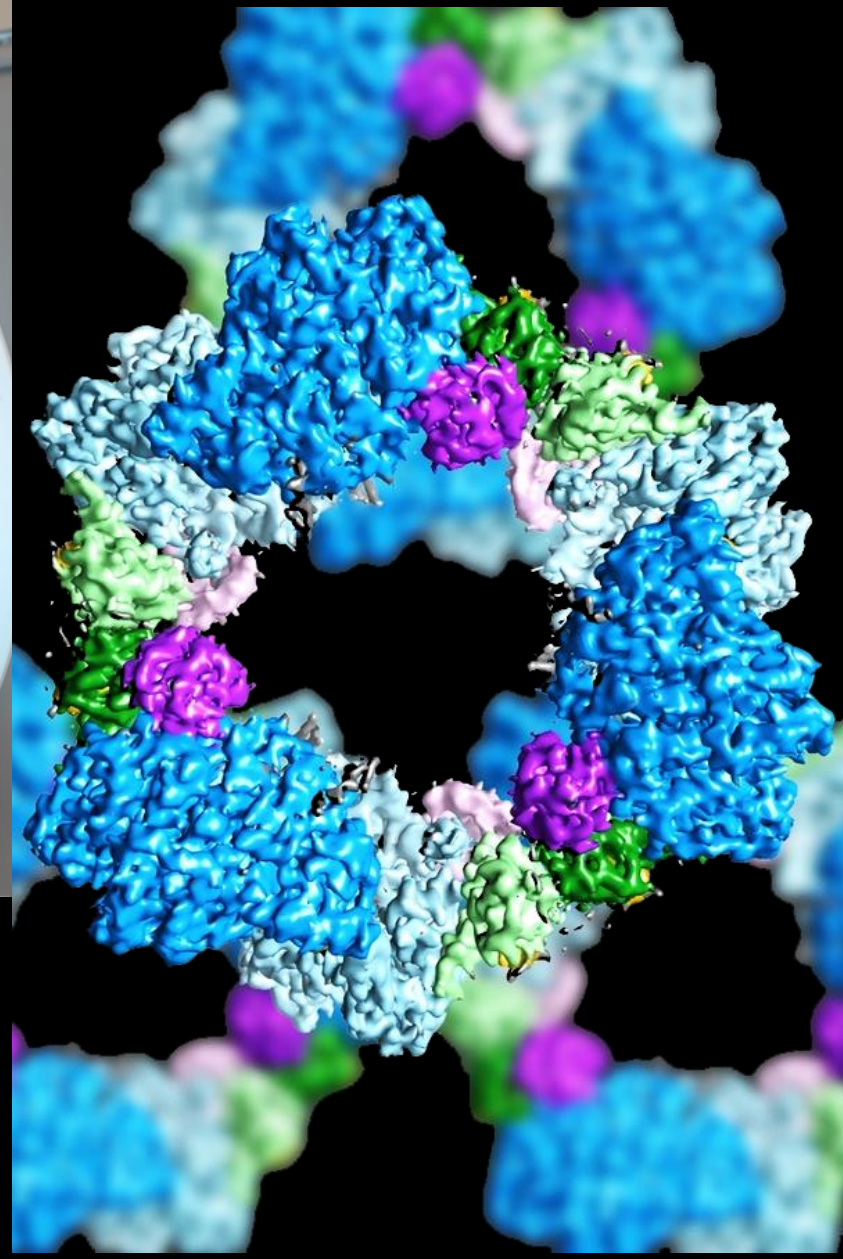
$$k = \frac{\sqrt{2m(V_0 - E)}}{\hbar}$$

Ψ_{inc}	Incident wave approaching the barrier
Ψ	Wave function inside the barrier (decays exponentially)
Ψ_{trans}	Transmitted wave after tunneling through the barrier
V_0	Height of the potential barrier



Nick Crawford

Independent quantum biochemist



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The glucose ketone index: a proposed quantitative biomarker to support cancer and chronic disease prevention and management

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Abstract

The chronic disease burden is rapidly becoming the most significant health challenge of the 21st century. Chronic noncommunicable diseases (NCDs) are replacing infectious diseases as the most significant factor in poor global health outcomes. NCDs account for 75% of disability adjusted life years. Cancer is one of the deadliest chronic diseases and is now on the verge of overtaking heart disease as the leading cause of death in the United States. Mitochondrial dysfunction linked to nutritional imbalance, lack of physical activity, and exposure to a broad range of environmental toxins is implicated in cancer and many chronic diseases. Although nutrition and exercise recommendations have been emphasized for primary prevention, overall health remains poor due to conflicting information and the inability to easily assess adherence. The glucose ketone index (GKI) was originally developed as a quantitative point-of-care blood biomarker for assessing diet adherence in cancer therapy. However, the ratio of gluose to ketones (specifically β-hydroxybutyrate) can also be linked to the risk of chronic diseases and may help predict risk more accurately than the glucose reading alone. Low GKI ratios are hypothesized to decrease risk, while high GKI are hypothesized to increase risk. Non-insulin-compensated euglycemia may help reduce chronic inflammation, insulin resistance, and pro-tumorigenic pathways. Endogenous ketone production reduces glucose requirements while simultaneously enhancing the bioenergetic

This talk is intended for educational purposes only and should not be taken as medical advice.

There are some cancers for which the metabolic approach is not appropriate

DNA MUTATIONS

1. Oncogenes – more than 200



DNA MUTATIONS

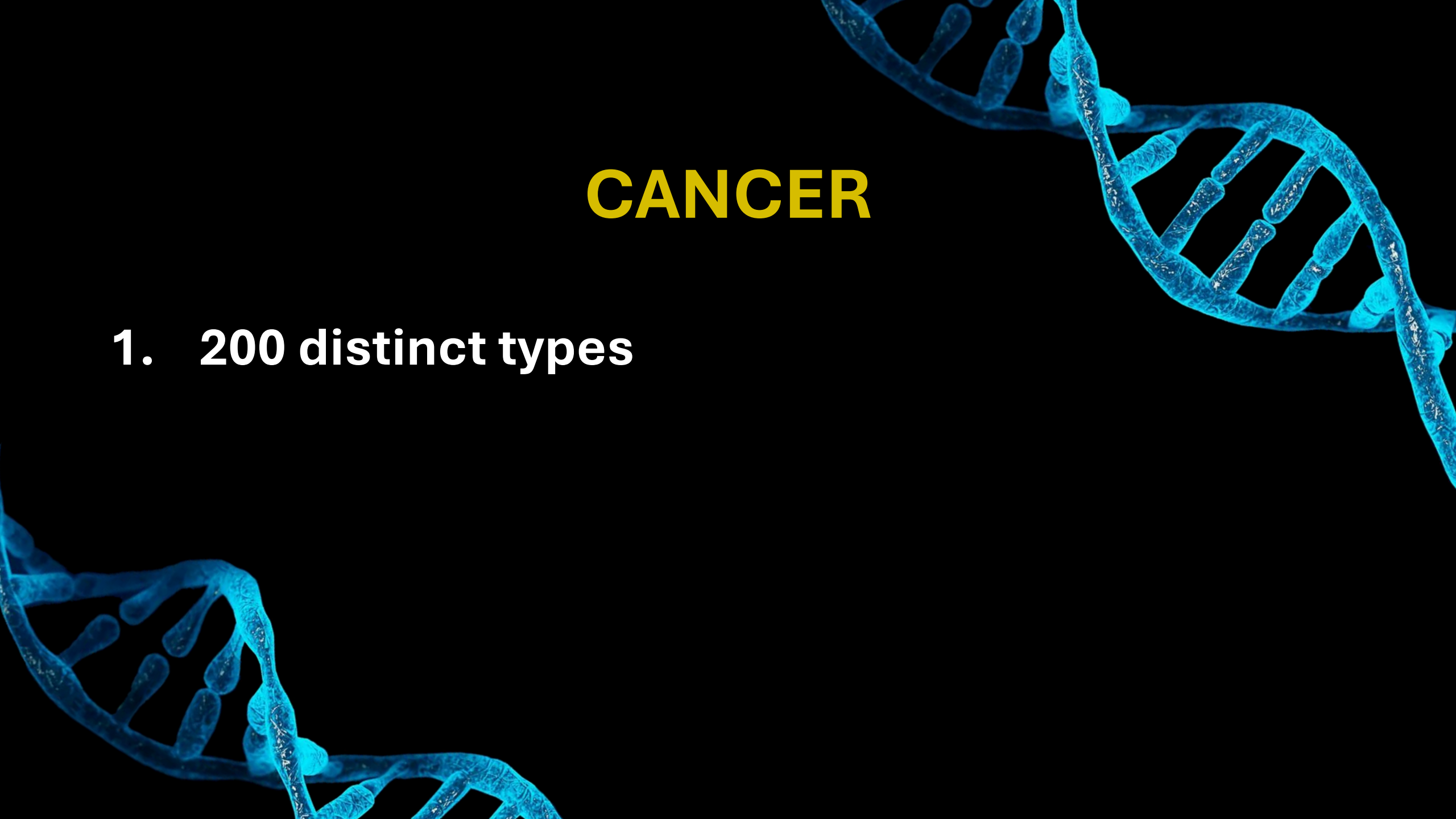
1. Oncogenes – more than 200
2. Tumour suppressor genes - more than 1,000



DNA MUTATIONS

1. Oncogenes – more than 200
2. Tumour suppressor genes - more than 1,000
3. DNA repair (caretaker) genes – more than 150





CANCER

1. 200 distinct types



CANCER

1. 200 distinct types
2. Countless sub-types and variations



CANCER

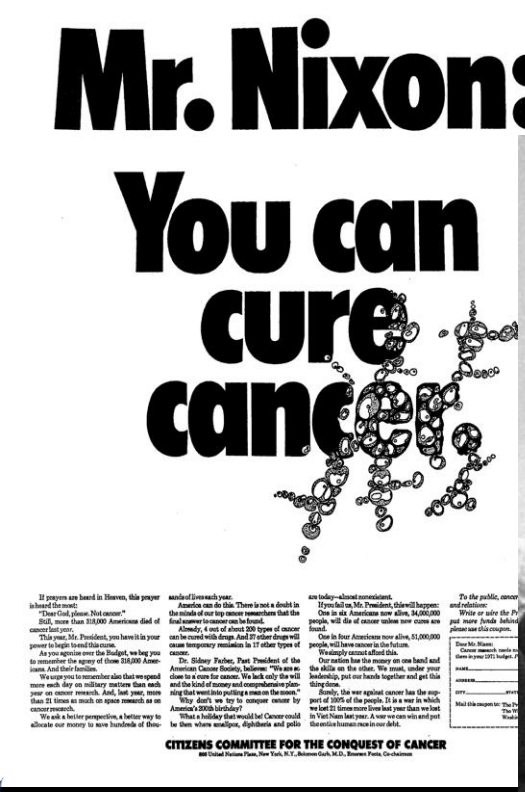
1. 200 distinct types
2. Countless sub-types and variations
3. Just about everyone’s cancer is different



With what looks like an almost limitless number of diseases...



...is it any wonder that progress has been frustratingly slow?







President Richard Nixon launched the "war on cancer" by signing the National Cancer Act of 1971 on December 23, 1971

GOV·UK

Home > Health and social care > Public health > Health conditions > Cancer research and treatment

Press release

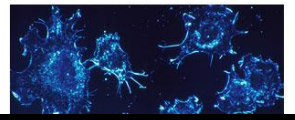
Health and Social Care Secretary to launch new 10-year ‘national war on cancer’

Health and Social Care Secretary Sajid Javid will launch a call for evidence to underpin an ambitious 10-Year Cancer Plan for England.

From: Department of Health and Social Care, Maria Caulfield and The Rt Hon Sajid Javid

Published: 4 February 2022

This was published under the 2019 to 2022 Johnson Conservative government





THE STANDARD

NEW

seeks views ‘from far and

‘war on

Health ary wants t e England cer ca best in Europe r diagno pped by 0 during ndemic.



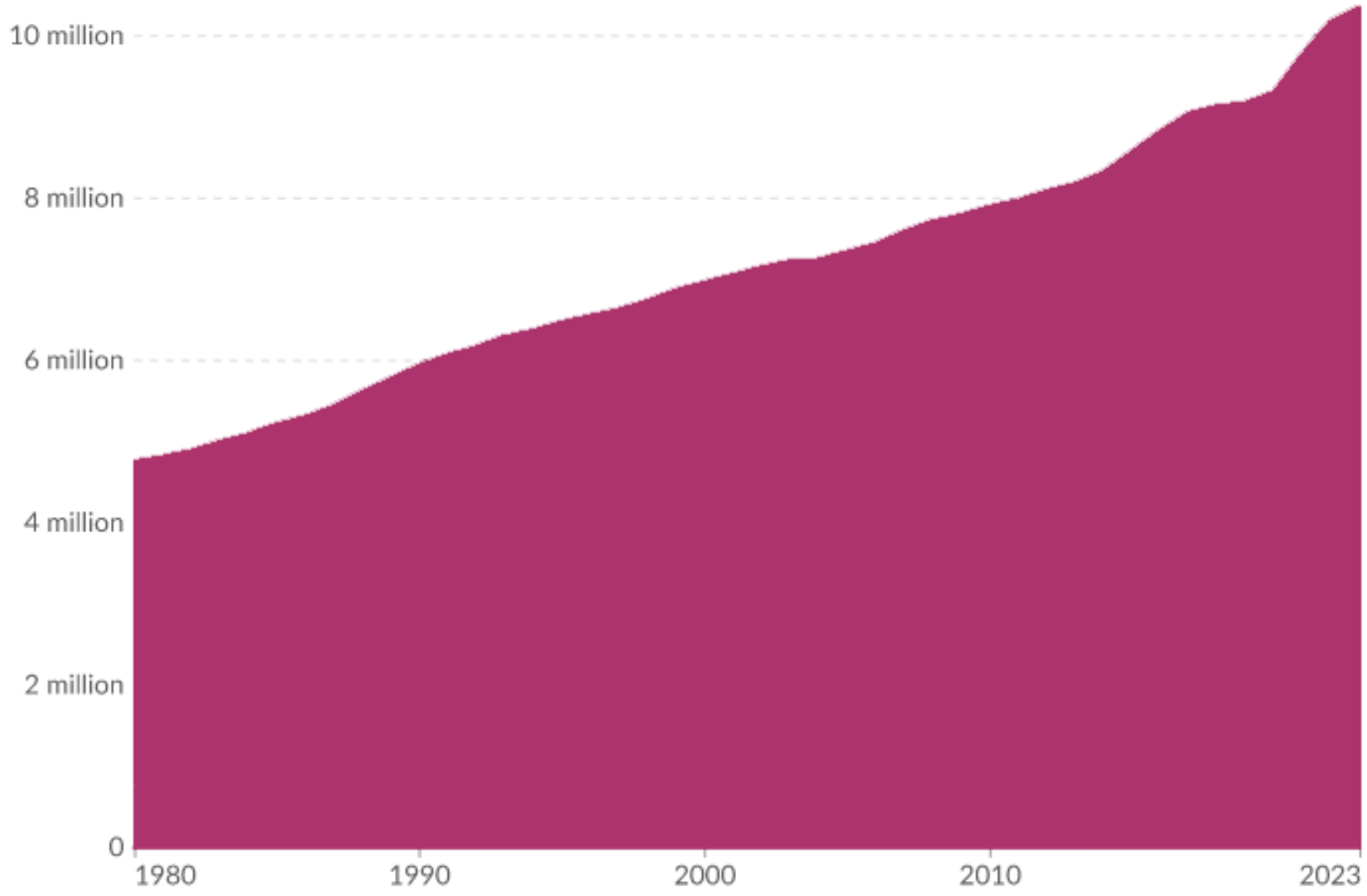
EALTH SECRETARY, SAJID JAVID VISITS ST GEORGE'S HOSPITAL IN SOUTH WEST NDON WHERE HE TALKED TO STAFF AND MET COVID 19 PATIENTS WHO ARE BEING ATED WITH A NEW ANTI-VIRAL DRUG. THE CORONAVIRUS BOOSTER PROGRAMME NTINUES ACROSS THE UK WITH THE GOVERNMENT'S AIM TO OFFER EVERYONE A OSTER JAB BY THE END OF THE YEAR. PICTURE DATE: WEDNESDAY DECEMBER 22, 2021.

PA WIRE

NINA LLOYD
4 FEBRUARY 2022

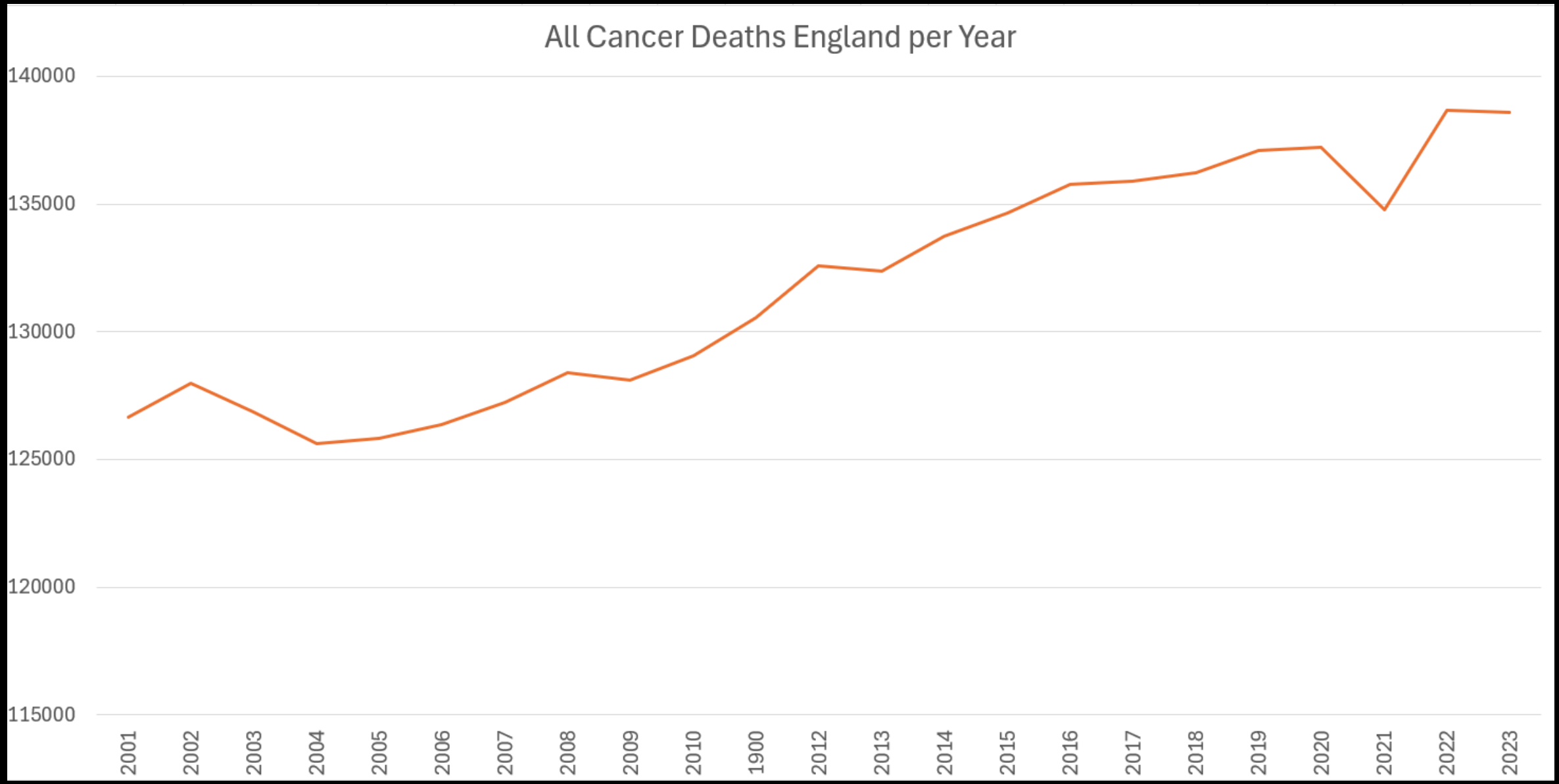
Heath Secretary Sajid Javid launching the UK’s "war on cancer" at the Francis Crick Institute on 4 February 2022.

Total Cancer Deaths Worldwide



Data source: IHME, Global Burden of Disease (2025)

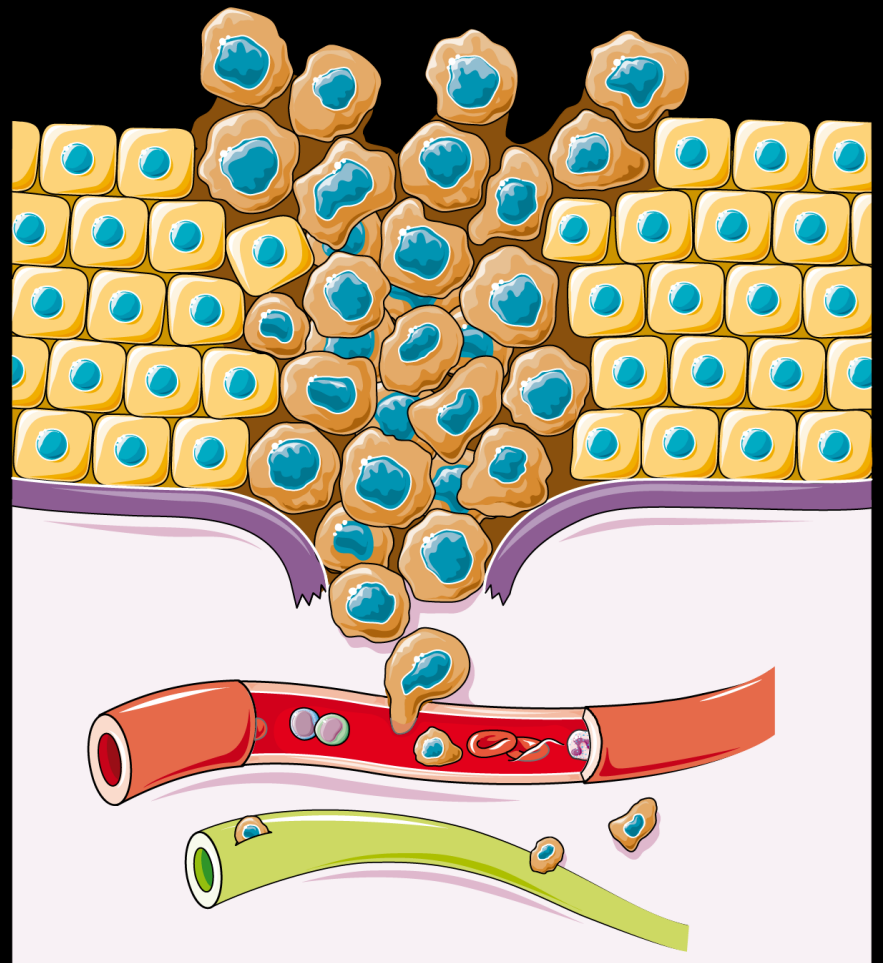
OurWorldinData.org/cancer | CC BY



Data from NHS England

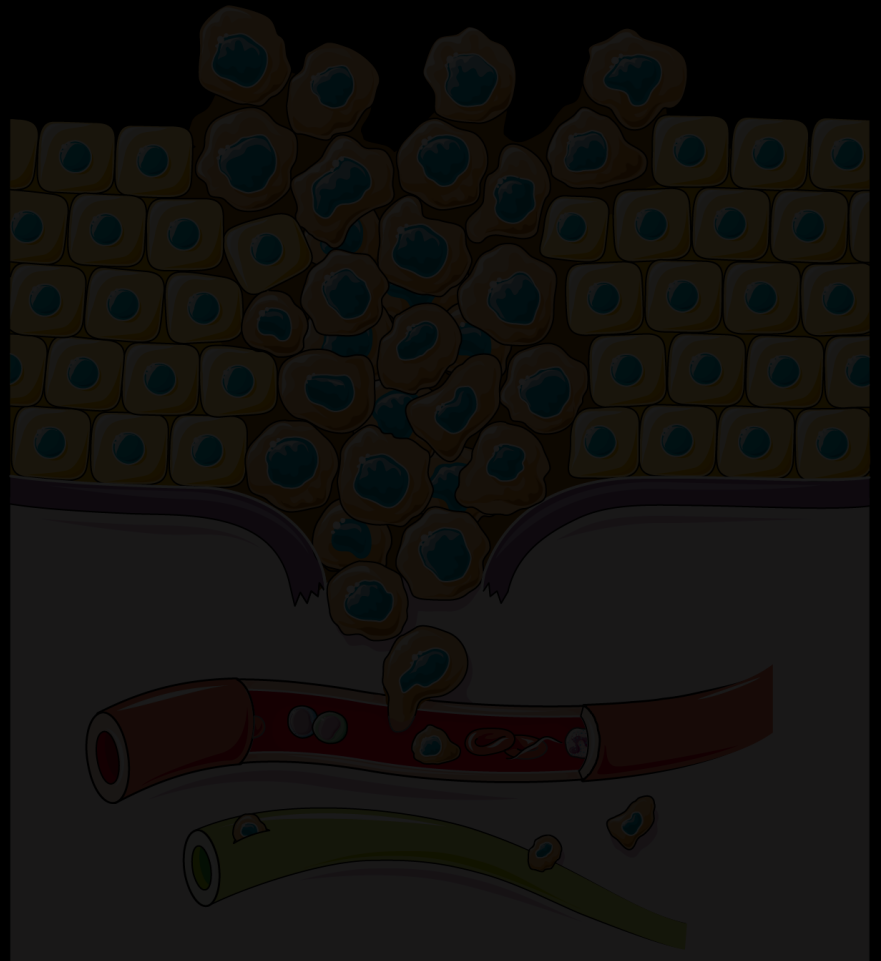


Otto Heinrich Warburg (1883 – 1970)




250 ml
GLUCOSEDRINK
Oral Glucose Tolerance Test Solution
75 g
glucose

X 100

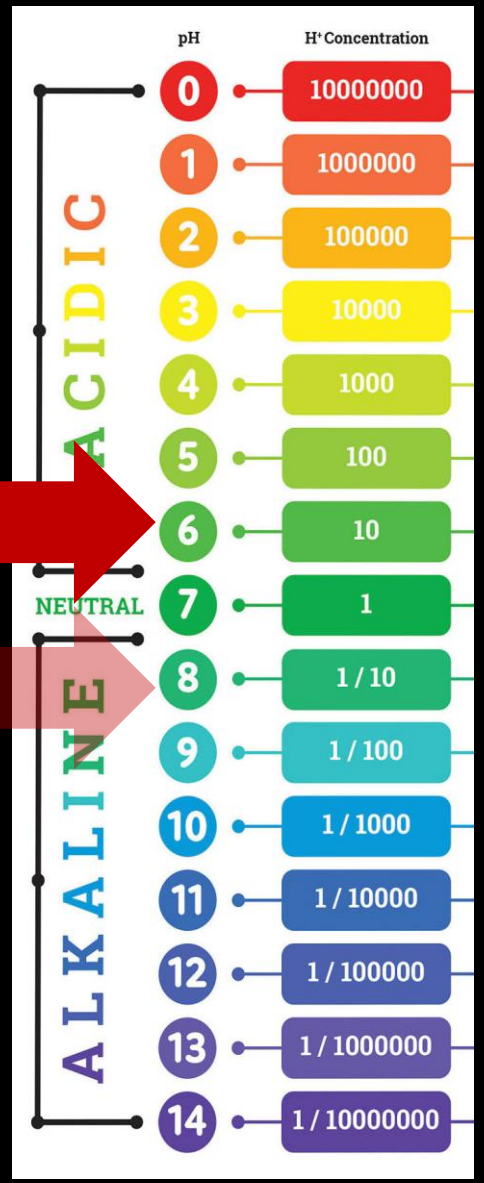




X 100

To 6.5

From 7.3





X 100



To 6.5

From 7.3

Lactic Acid
&
Succinic Acid





X 100



To

Fr

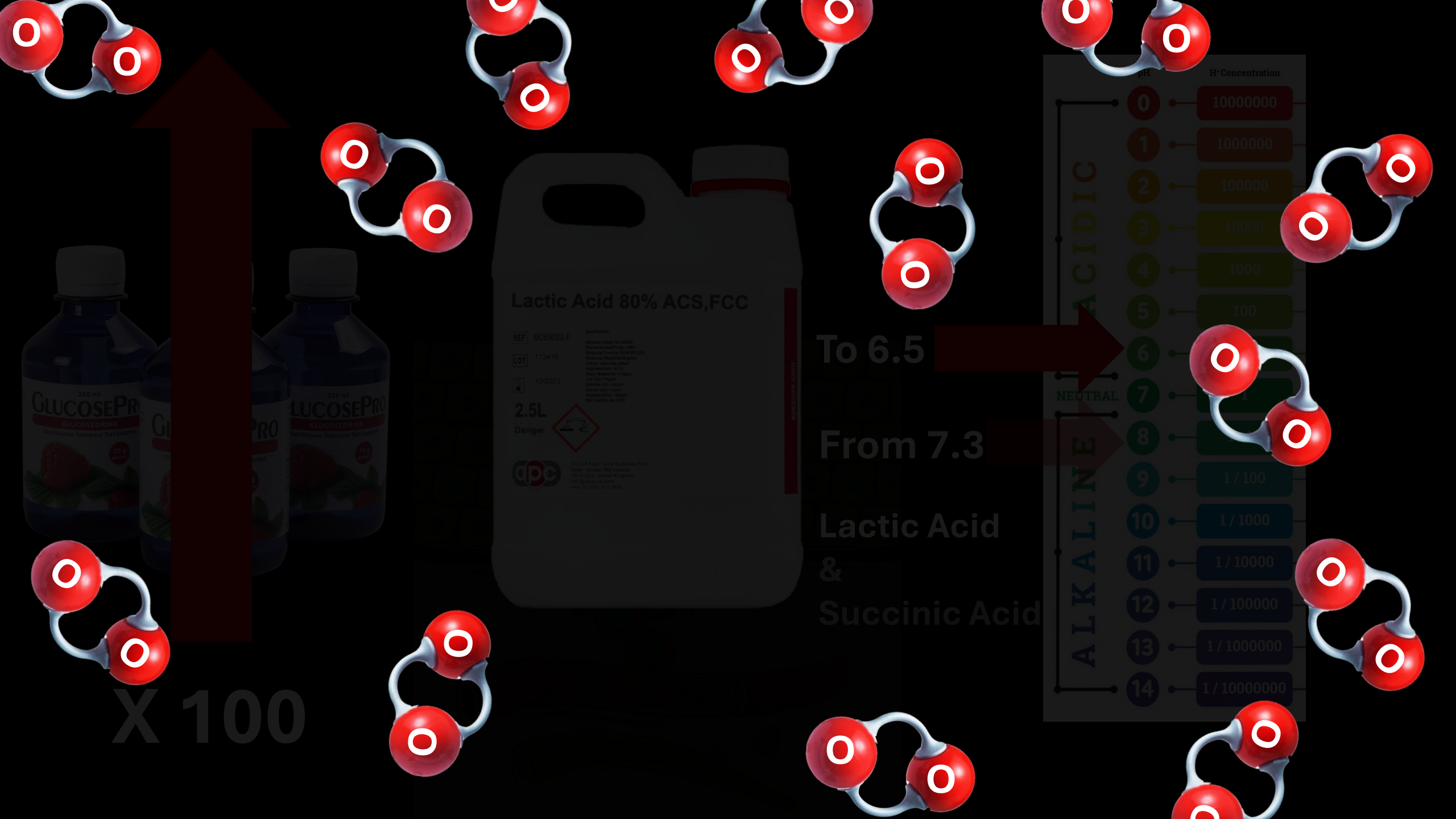
La

&

Succinic Acid

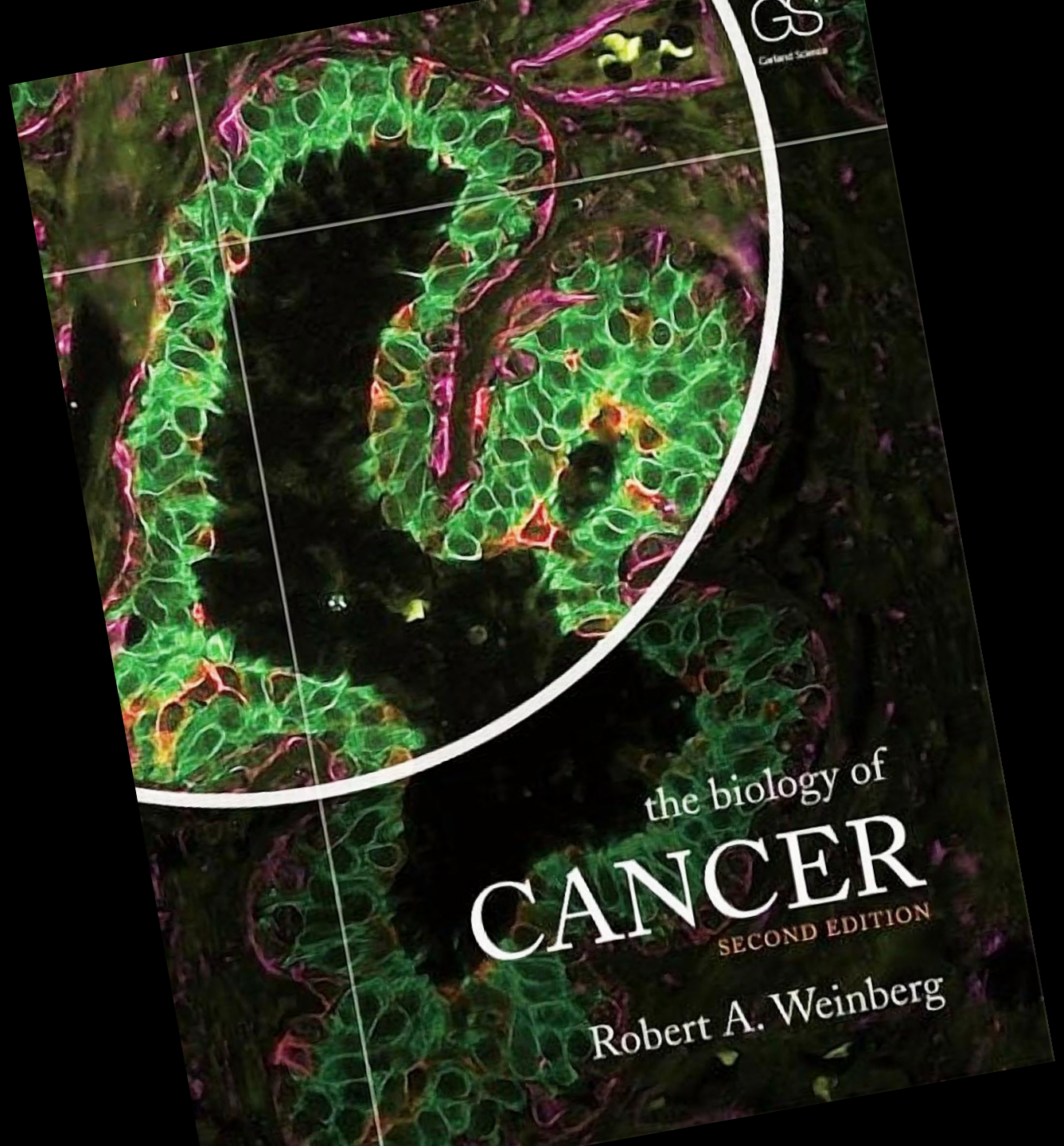





X 100
Lactic Acid 80% ACS,FCC
2.5L
Danger
To 6.5
From 7.3
Lactic Acid
&
Succinic Acid
ACIDIC
NEUTRAL
ALKALINE
pH
H+ Concentration
0 10000000
1 1000000
2 100000
3 10000
4 1000
5 100
6
7
8
9 1 / 100
10 1 / 1000
11 1 / 10000
12 1 / 100000
13 1 / 1000000
14 1 / 10000000


X 100
Lactic Acid 80% ACS,FCC
To 6.5
From 7.3
Lactic Acid
&
Succinic Acid
pH
H+ Concentration
ACIDIC
NEUTRAL
ALKALINE
0 10000000
1 1000000
2 100000
3 10000
4 1000
5 100
6
7
8
9 1 / 100
10 1 / 1000
11 1 / 10000
12 1 / 100000
13 1 / 1000000
14 1 / 10000000


250 ml
GLUCOSEDRINK
Oral Glucose Tolerance Test Solution
75 g
Lactic Acid 80% ACS,FCC
ECE9022-F
113418
To 6.5
From 7.3
pH
H⁺ Concentration
ACIDIC
NEUTRAL
ALKALINE
0 10000000
1 1000000
2 100000
3 10000
4 1000
5 100
6
7
8
9 1 / 100
10 1 / 1000
11 1 / 10000
12 1 / 100000
13 1 / 1000000
14 1 / 10000000
X 100



‘The most widely read and definitive academic textbook on cancer biology is *The Biology of Cancer* by Robert A. Weinberg.’

‘Most read cancer biology book?’
Google AI 24 September 2026

make little sense energetically, since the breakdown of one molecule of glucose yields only two molecules of ATP through glycolysis. In contrast, when under aerobic conditions glycolysis is followed by oxidation of pyruvate in the citric acid cycle, as many as 36 ATPs per glucose molecule are generated. In fact, most types of normal cells in the body have continuous access to O_2 conveyed by the blood and therefore metabolize glucose through this energetically far more efficient route. The tendency of cancer cells to limit themselves to glycolysis, even when provided with adequate oxygen, stands out as exceedingly unusual behavior.

The fact that cancer cells metabolize glucose so inefficiently requires them to compensate by importing enormous amounts of glucose. This behavior is seen in many types of cancer cells, including both carcinomas and hematopoietic tumors; they express greatly elevated levels of glucose transporters, particularly GLUT1, which span the plasma membrane and drive the high rates of glucose uptake by these cells. Radiolo-

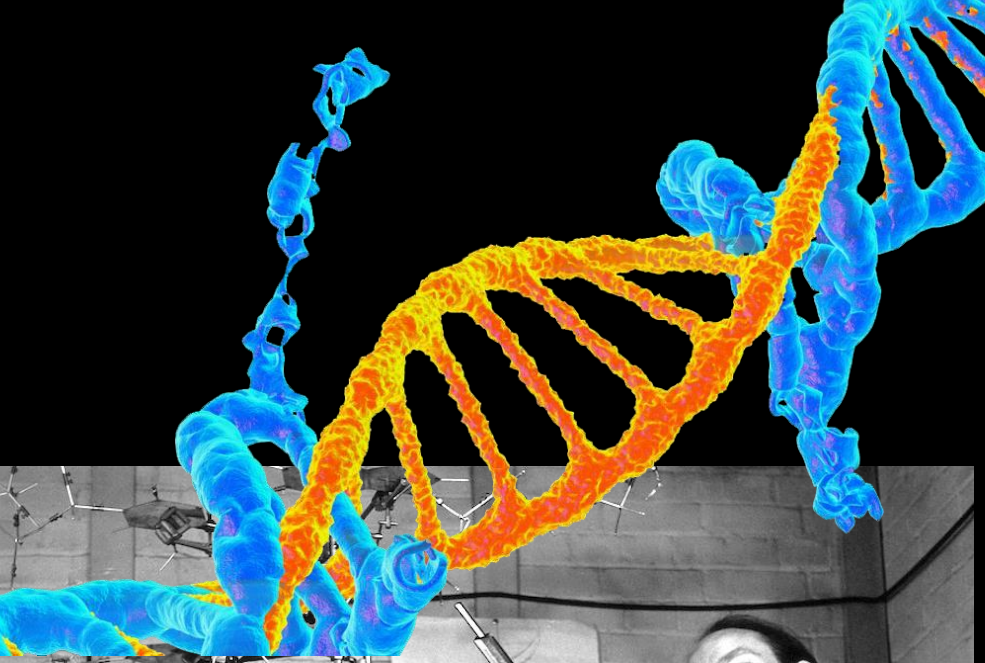
“Exceedingly unusual behaviour”

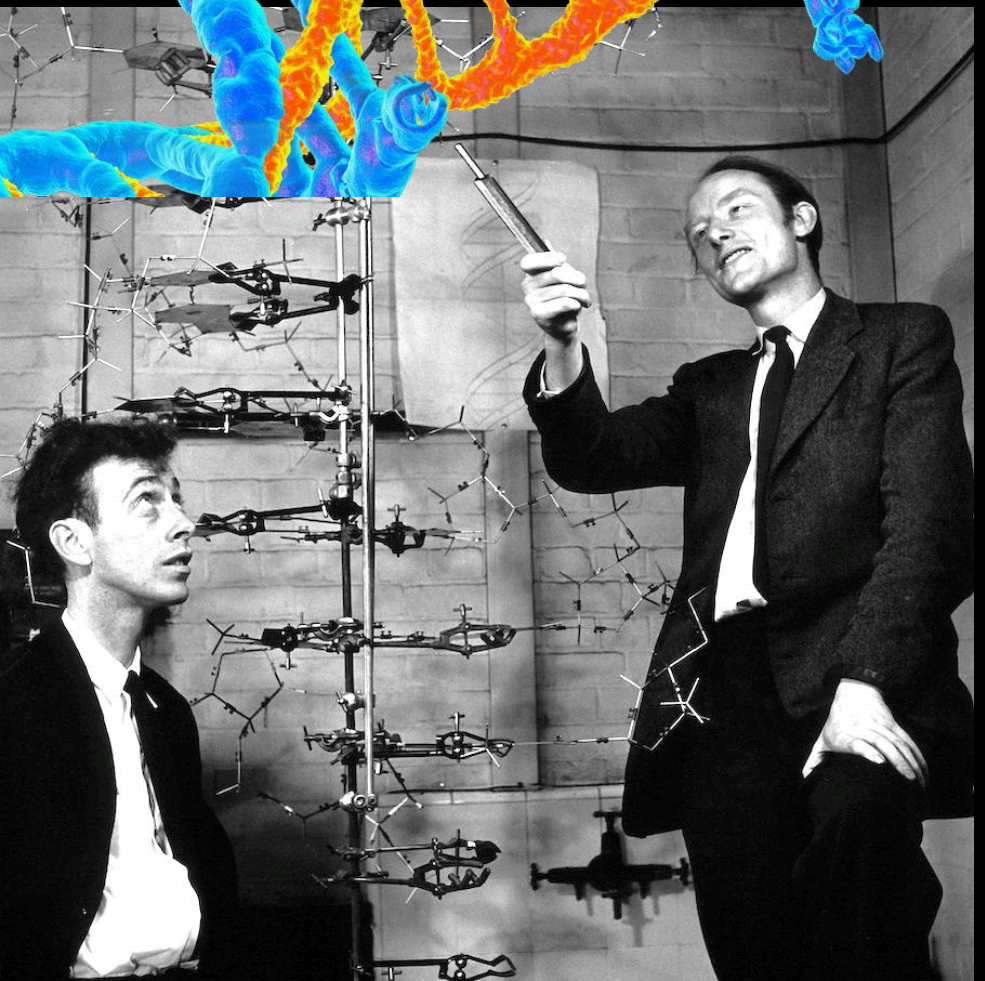
Robert A. Weinberg, The Biology of Cancer, 2nd ed. 2014. pp53.

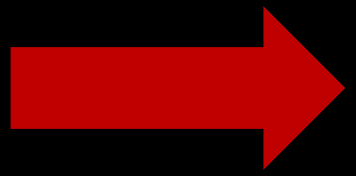
concentration in tumors (see Figure 2.22C).

In the 1950s, Warburg proposed that this altered energy metabolism was the driving force in the formation of cancer cells, a notion that was discredited in the decades that followed. However, the process of aerobic glycolysis that he discovered was ultimately found to operate in a wide variety of human cancer cells and is now thought to represent one of the many consequences of cell transformation.

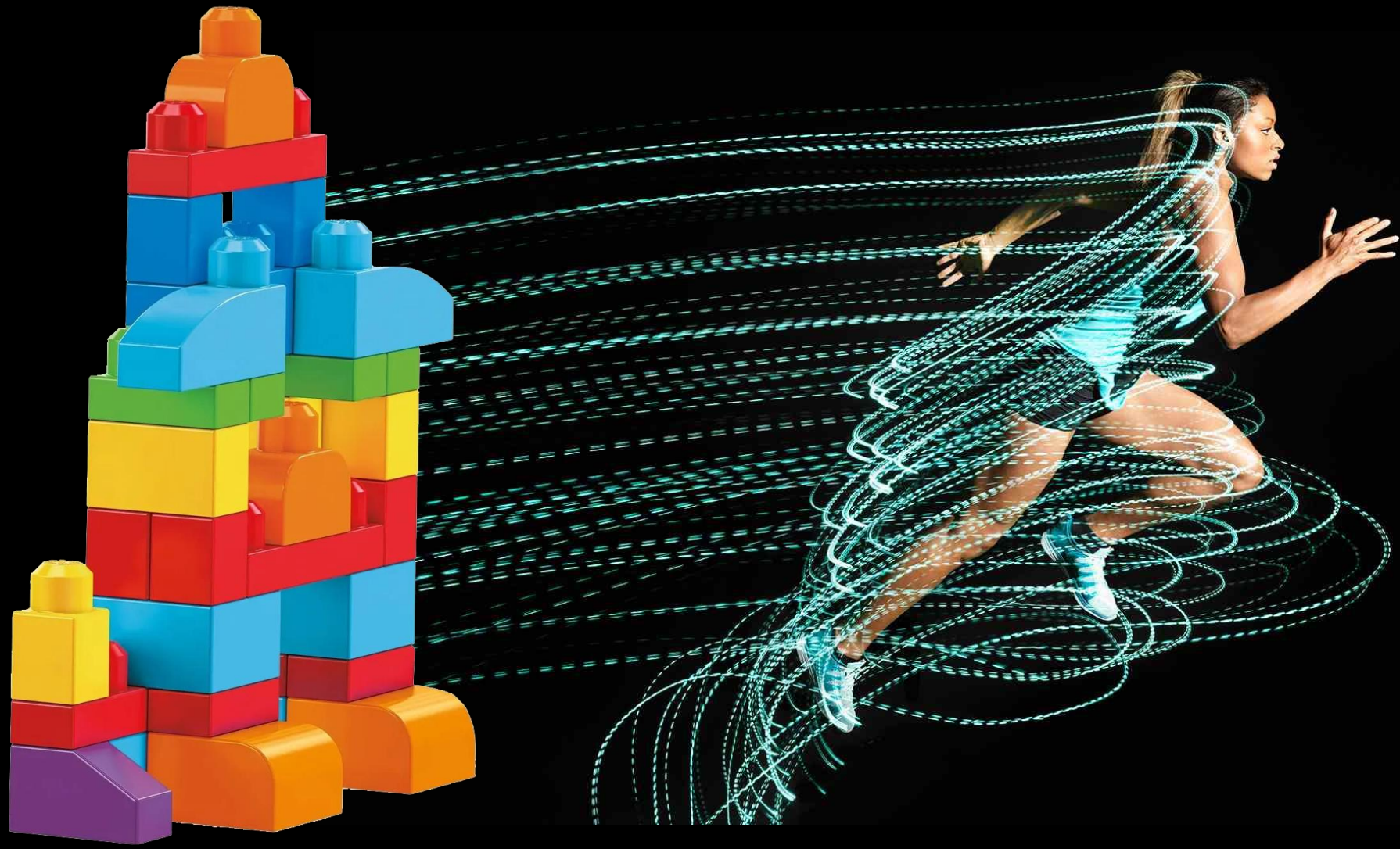
Aerobic glycolysis, sometimes called the **Warburg effect**, remains a subject of much contention, as its rationale in cancer cell biology has never been fully resolved: why do as many as 80% of cancer cells metabolize most of their glucose via glycolysis when completion of glucose degradation in mitochondria by the citric acid cycle would afford them vastly more ATP to fuel their own growth and proliferation? Is aerobic








Otto Warburg 1883-1970
50
DEUTSCHE BUNDESPOST
1983

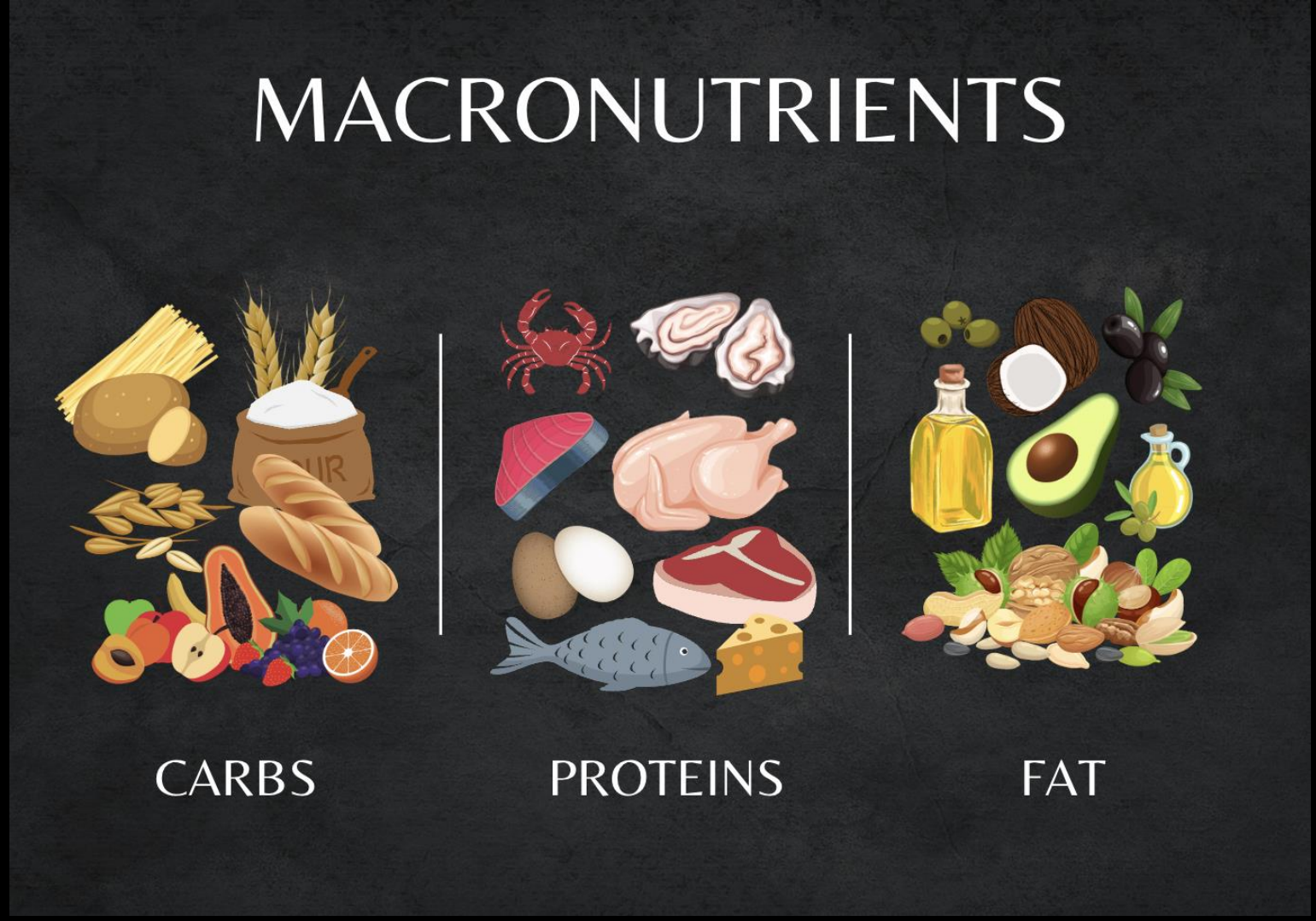


Building Blocks & Energy

MACRONUTRIENTS



CARBS PROTEINS FAT



+ OXYGEN + WATER

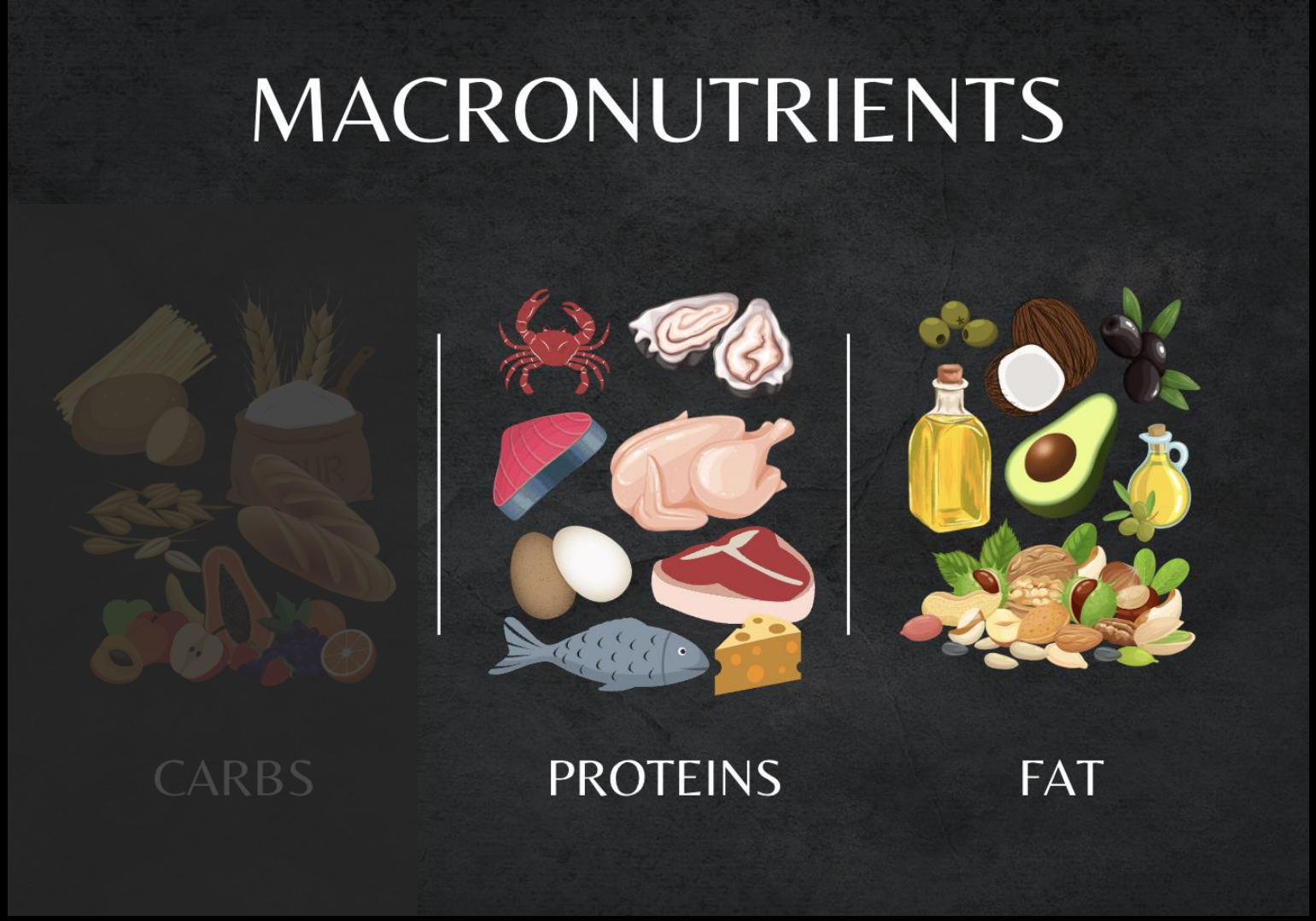




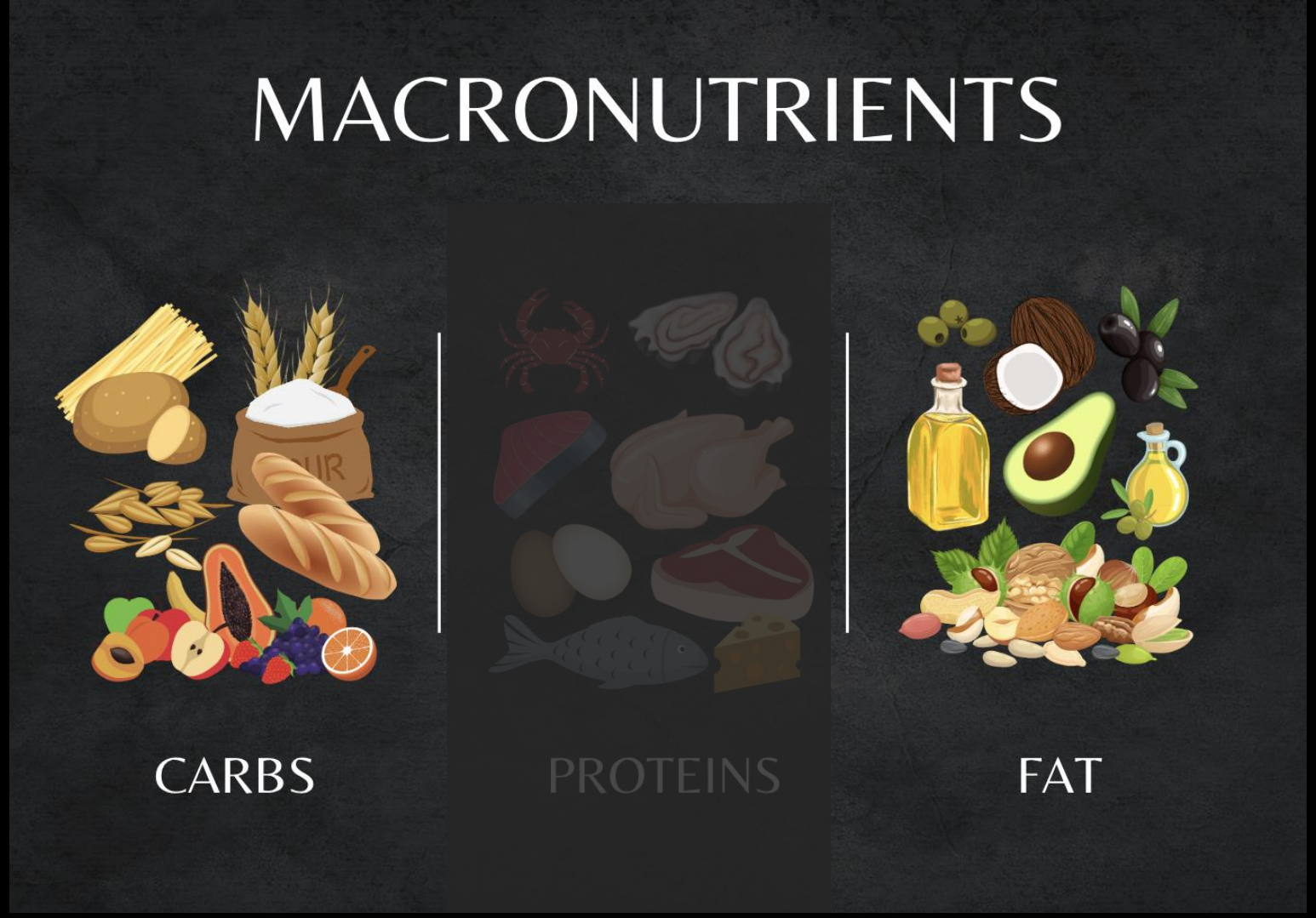


The Hidden Macronutrient

Fibre



Building Blocks



Energy

Eatwell Guide

Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.

Check the label on packaged foods

Each serving (150g) contains

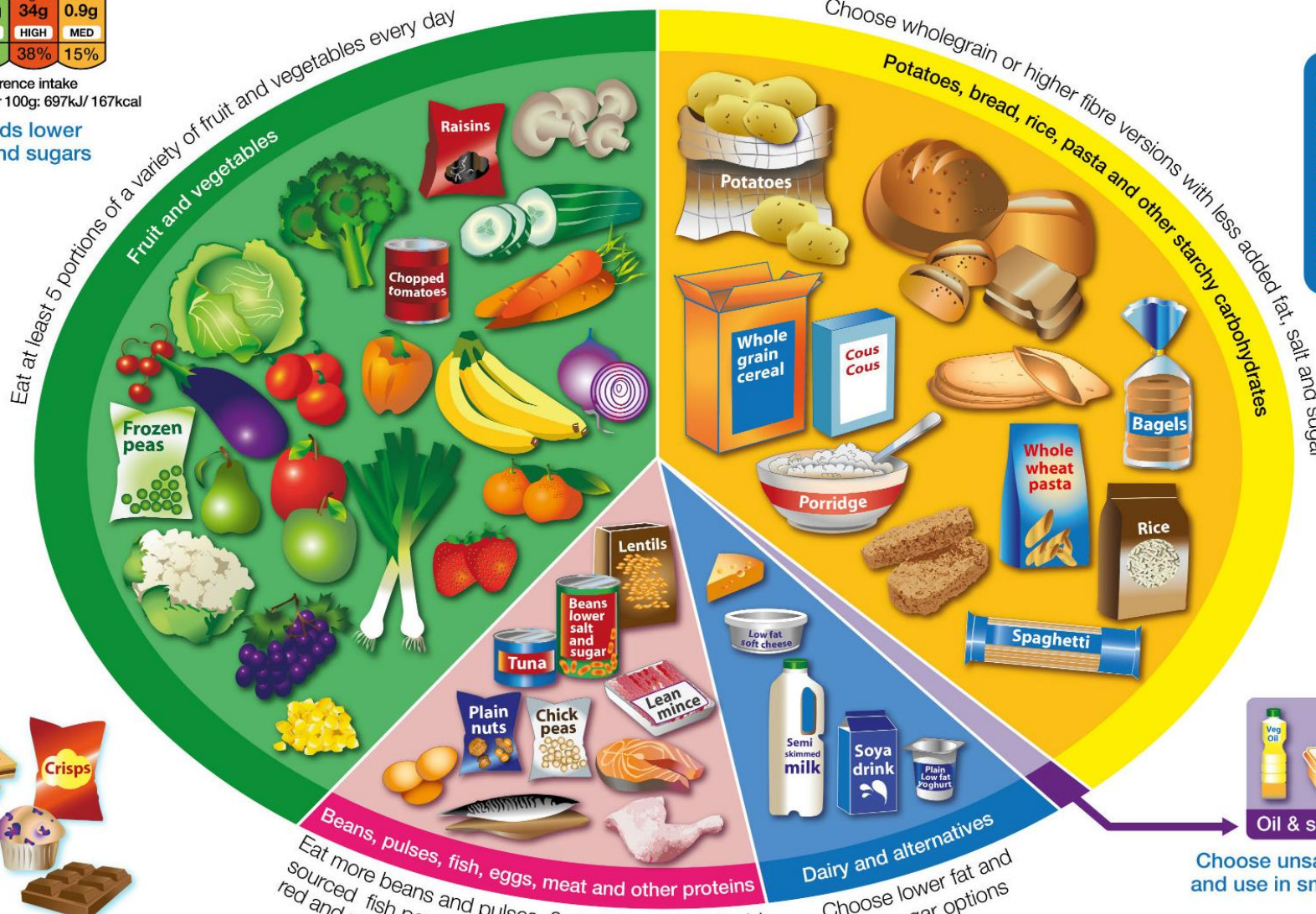
Energy	Fat	Saturates	Sugars	Salt
1046kJ 250kcal	3.0g	1.3g	34g	0.9g
	LOW	LOW	HIGH	MED
13%	4%	7%	38%	15%

of an adult's reference intake
Typical values (as sold) per 100g: 697kJ/ 167kcal

Choose foods lower in fat, salt and sugars



Eat less often and in small amounts



Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Choose lower fat and lower sugar options

Choose unsaturated oils and use in small amounts



Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

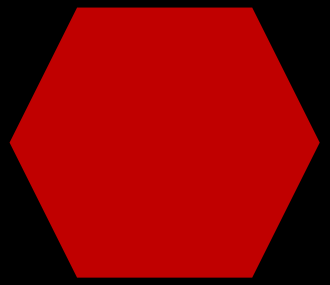


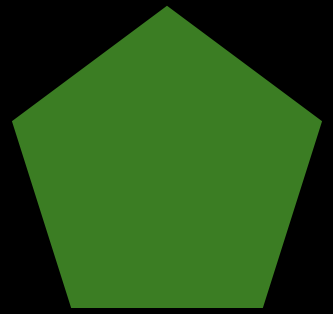
Energy













Glucose

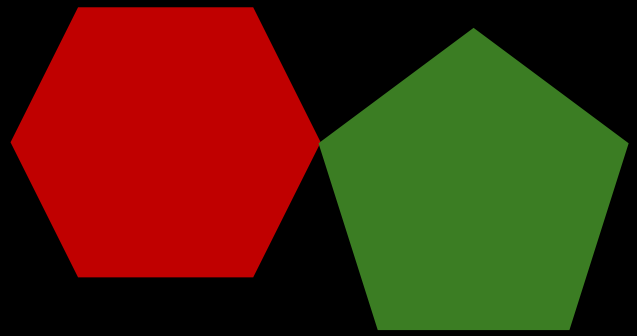
Fructose

Galactose



Starch





Glucose Fructose

Sucrose - Sugar







CARBS:
GLUCOSE + FRUCTOSE
















CARBS:
STARCH + SUGAR















CARBS:
GRAINS, POTATOES, FRUIT



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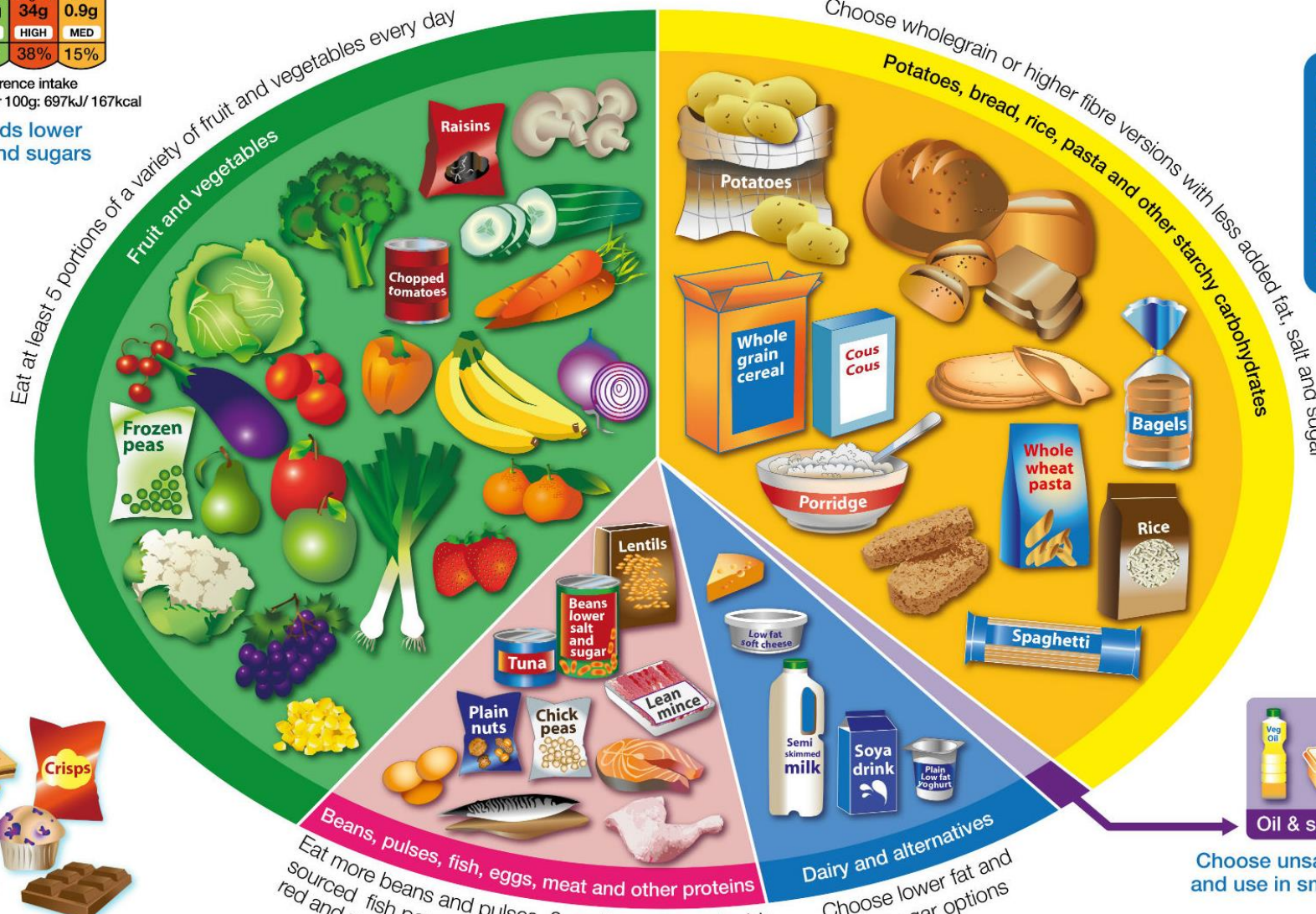

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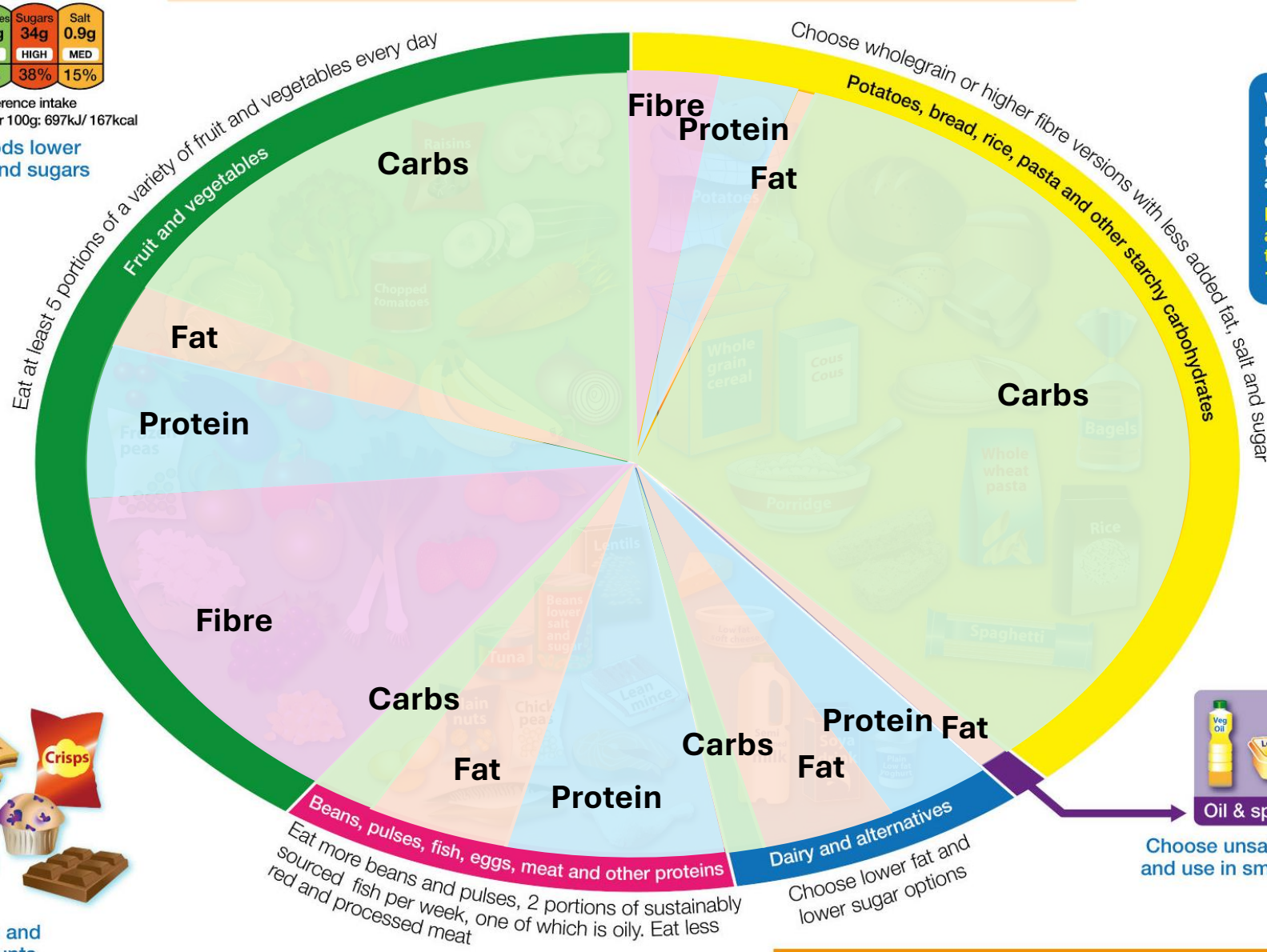



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Choose foods lower in fat, salt and sugars

Eat at least 5 portions of a variety of fruit and vegetables every day

Fruit and vegetables

Frozen peas

Carbs

Choose wholegrain or higher fibre versions with less added fat, salt and sugar

Potatoes, bread, rice, pasta and other starchy carbohydrates

Potatoes

Carbs

Beans, pulses, fish, eggs, meat and other proteins

Lentils

Beans lower salt and sugar

Tuna

Lean mince

Plain nuts

Chick peas

Carbs

Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Dairy and alternatives

Low fat soft cheese

Semi milk

Soya drink

Plain Low fat Yoghurt

Carbs

Choose lower fat and lower sugar options

Oil & spreads

Veg Oil

Lower fat spread

Choose unsaturated oils and use in small amounts

Sauce

Crisps

Eat less often and in small amounts

6-8 a day

Water, lower fat milk, sugar-free drinks including tea and coffee all count.

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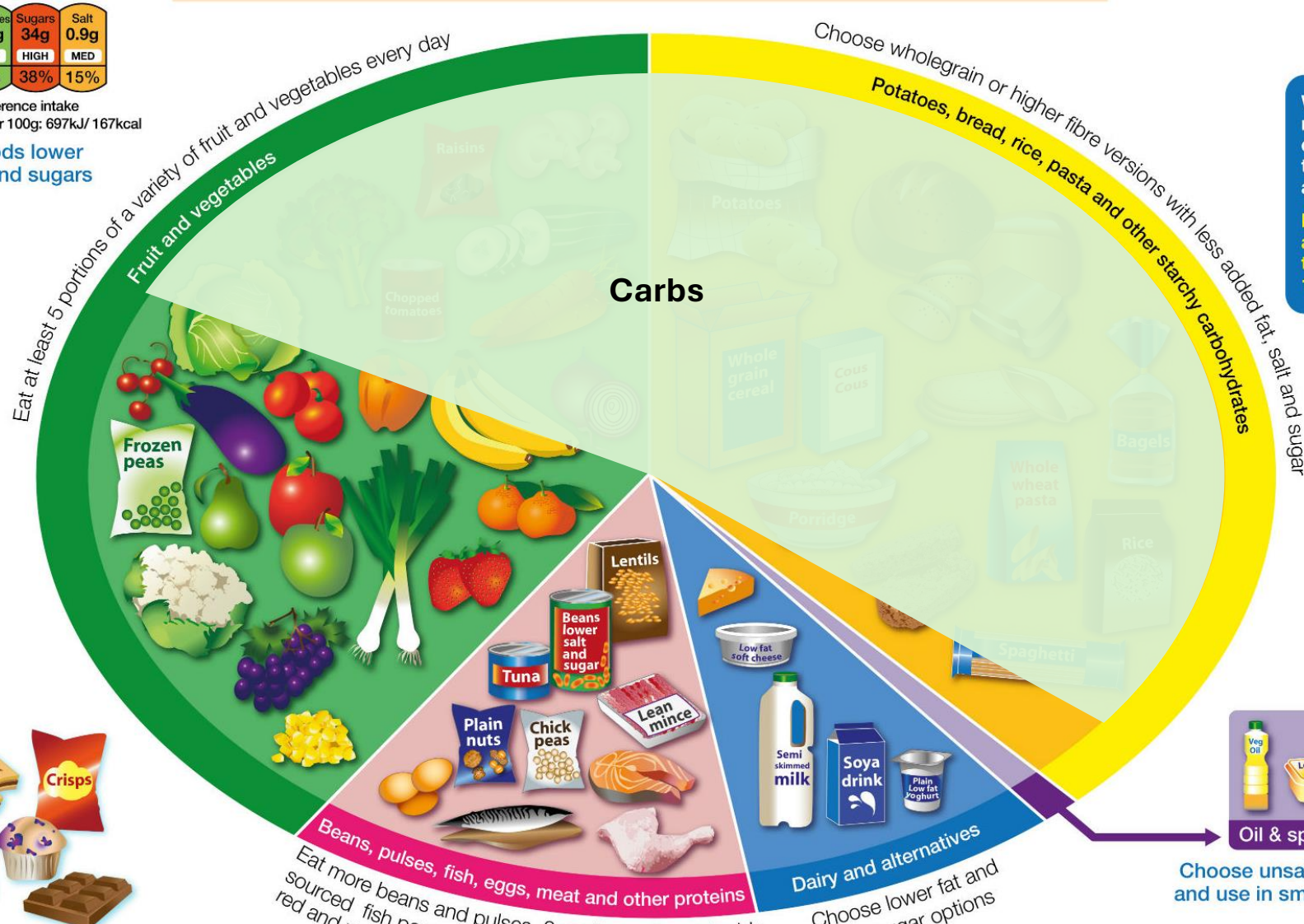

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13%	4%	7%	38%	15%

of an adult's reference intake

Typical values (as sold) per 100g: 697kJ/ 167kcal

Choose foods lower in fat, salt and sugars

Carbs



Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.



Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Choose lower fat and lower sugar options



Eat less often and in small amounts

Choose unsaturated oils and use in small amounts

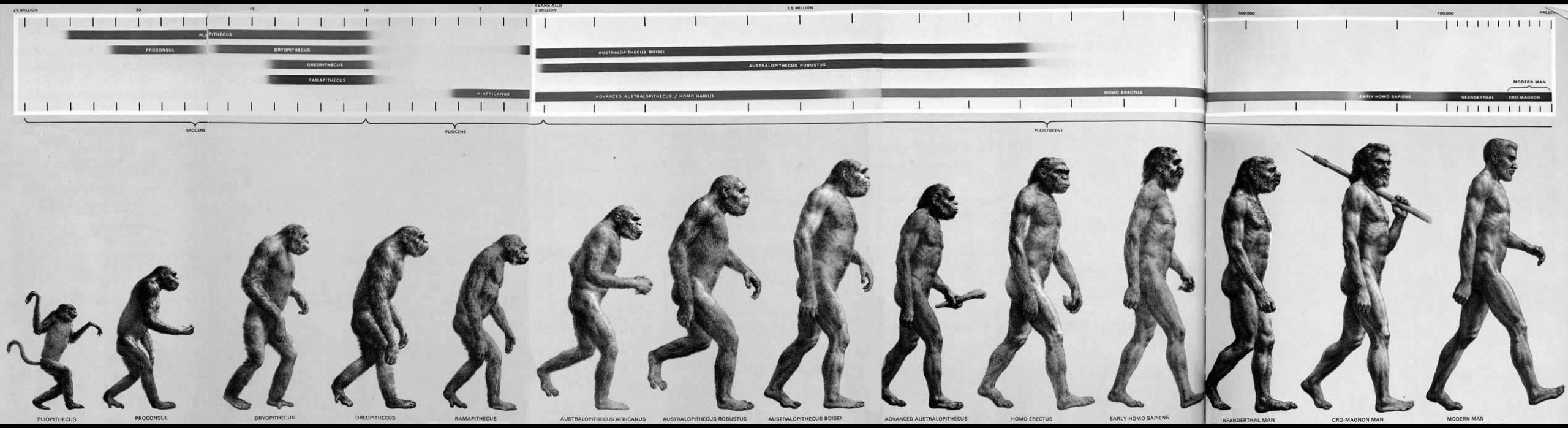
Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

That’s a bit strange considering Warburg’s findings regarding cancer and glucose.

Why are we being advised to eat large amounts of glucose when cancer feeds off glucose?

SANITY CHECK 1

What Does History Say About our Diet?


25 MILLION
20
15
10
5
YEARS AGO
2 MILLION
1.5 MILLION
500,000
100,000
PRESENT
PLIOPITHECUS
PROCONSUL
DRYOPITHECUS
OREOPITHECUS
RAMAPITHECUS
A. AFRICANUS
AUSTRALOPITHECUS BOISEI
AUSTRALOPITHECUS ROBUSTUS
ADVANCED AUSTRALOPITHECUS / HOMO HABILIS
HOMO ERECTUS
MODERN MAN
EARLY HOMO SAPIENS
NEANDERTHAL
CRO-MAGNON
MIOCENE
PLIOCENE
PLEISTOCENE
PLIOPITHECUS
PROCONSUL
DRYOPITHECUS
OREOPITHECUS
RAMAPITHECUS
AUSTRALOPITHECUS AFRICANUS
AUSTRALOPITHECUS ROBUSTUS
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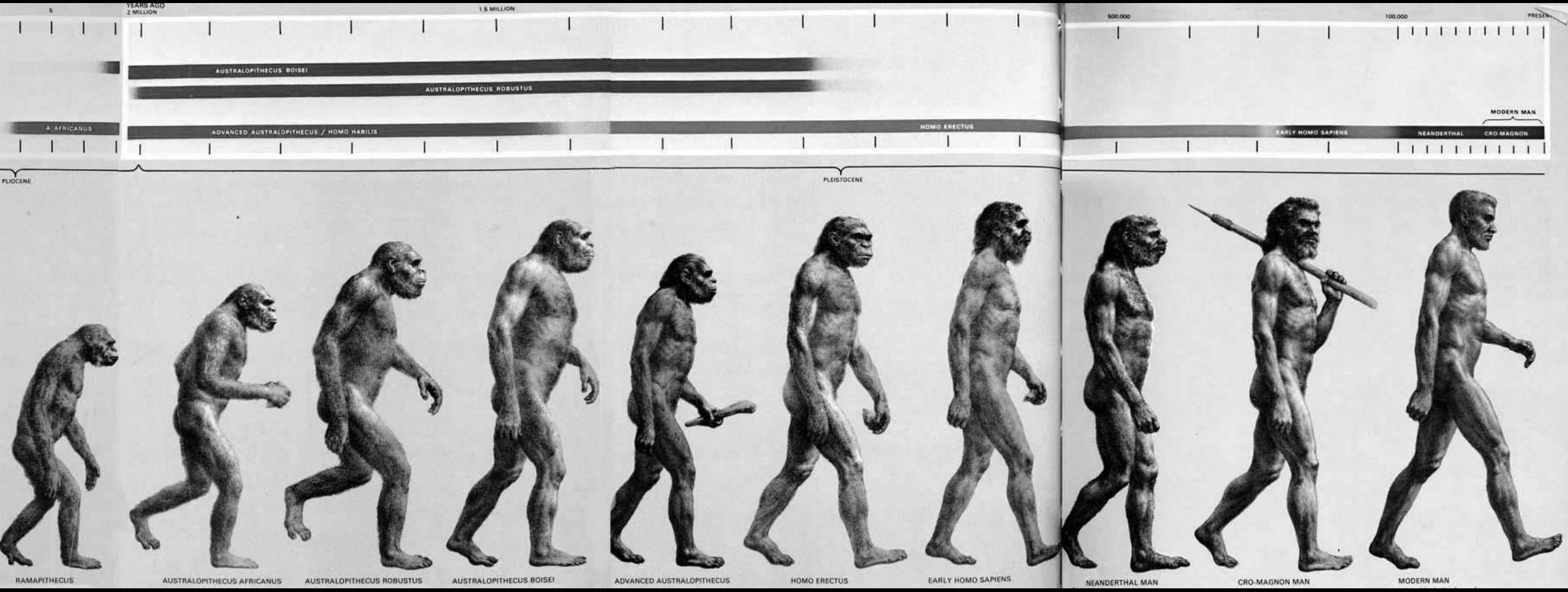
ADVANCED AUSTRALOPITHECUS
HOMO ERECTUS
EARLY HOMO SAPIENS
NEANDERTHAL MAN
CRO-MAGNON MAN
MODERN MAN

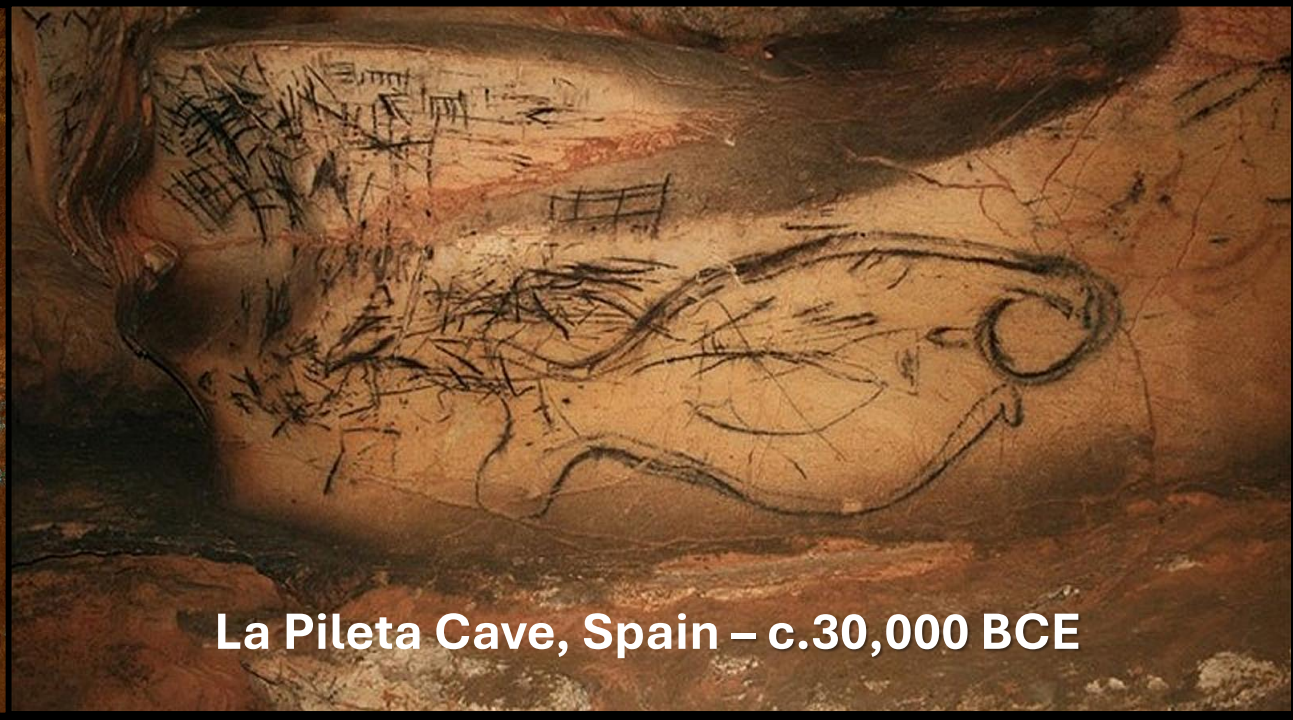


2.5 million years

100,000 generations


Hunter gatherers 2.5M – 10,000 BCE


Lascaux Hunting Scene – c.17,000 BCE

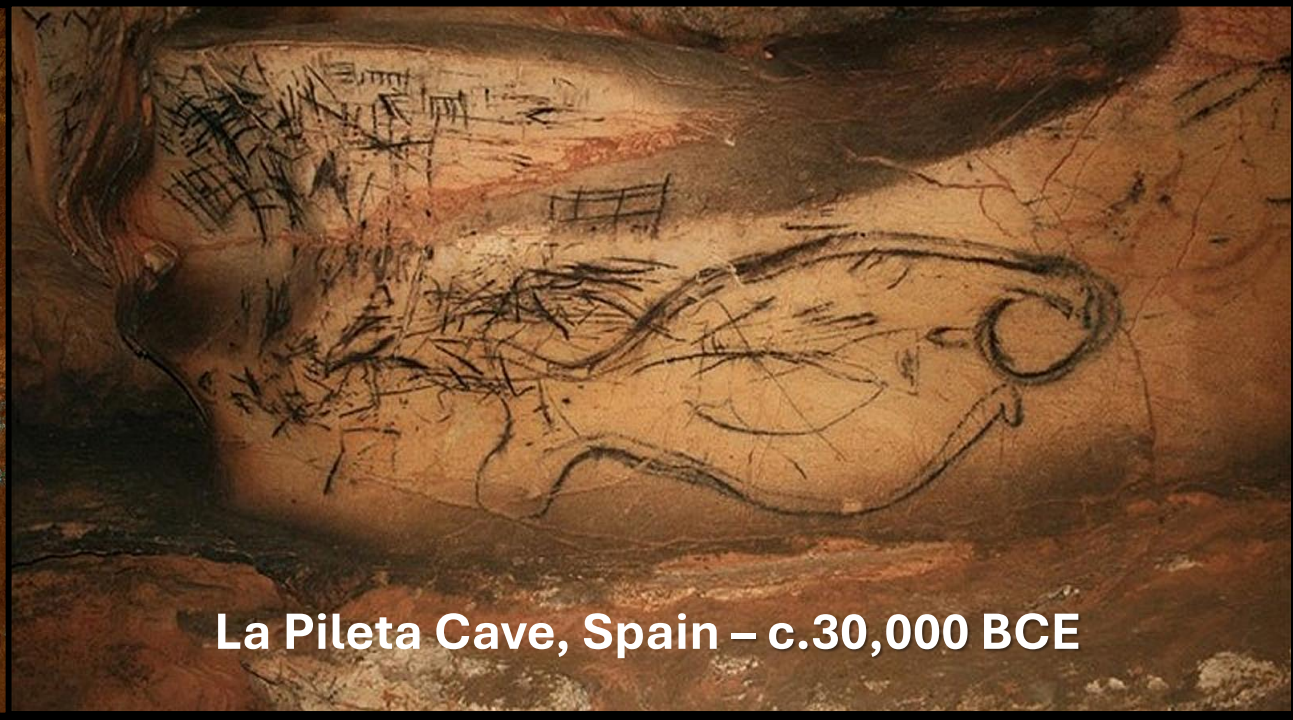

La Pileta Cave, Spain – c.30,000 BCE


Legumes, nuts and seeds


Leafy Greens


Fruit


Lascaux Hunting Scene – c.17,000 BCE


La Pileta Cave, Spain – c.30,000 BCE


Legumes, nuts and seeds


Leafy Greens


Fruit


Lascaux Hunting Scene – c.17,000 BCE


La Pileta Cave, Spain – c.30,000 BCE


Legumes, nuts and seeds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Lascaux Hunting Scene – c.17,000 BCE


La Pileta Cave, Spain – c.30,000 BCE


Legumes, nuts and seeds


Leafy Greens


Fruit


Lascaux Hunting Scene – c.17,000 BCE


La Pileta Cave, Spain – c.30,000 BCE


Legumes, nuts and seeds


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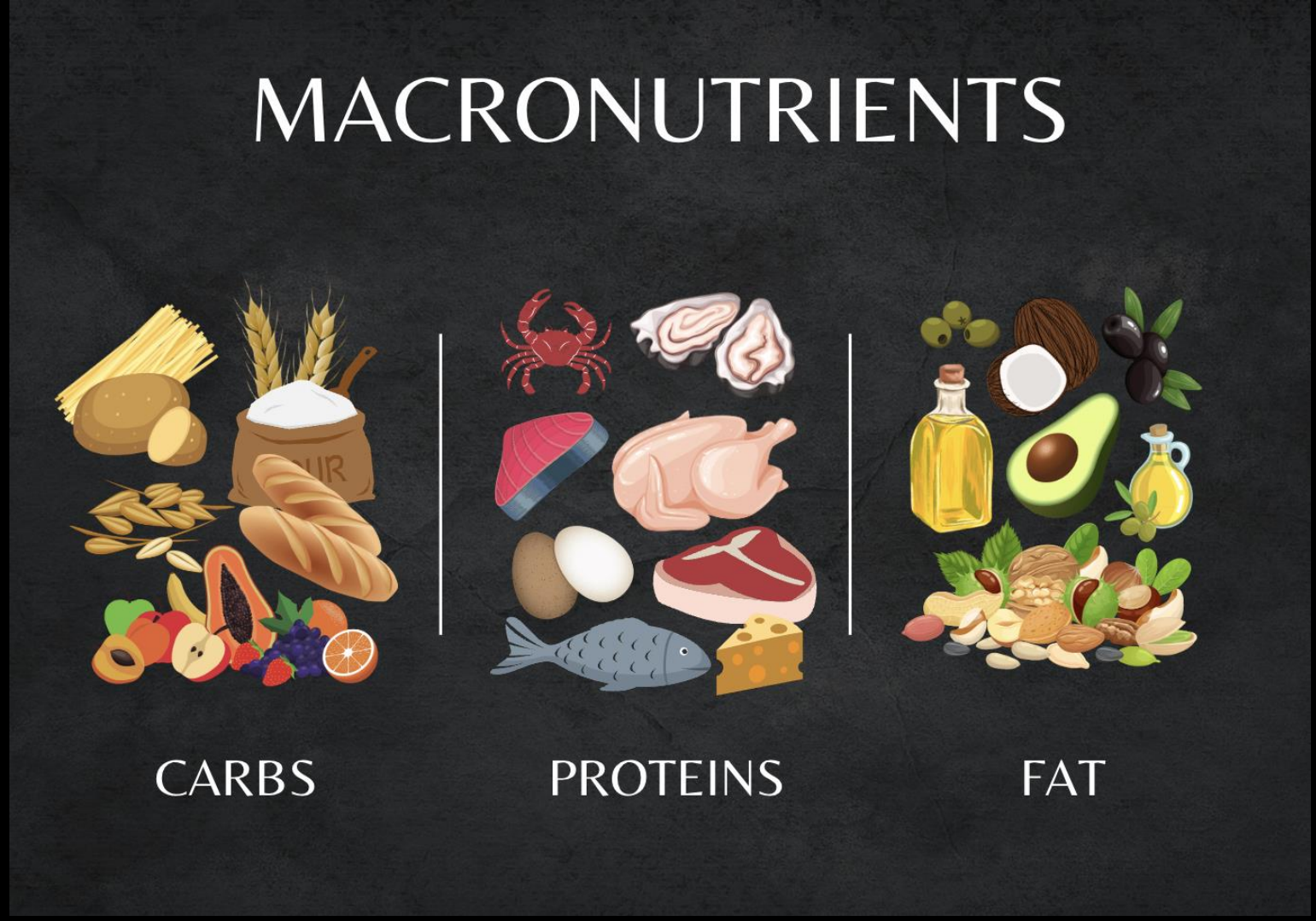
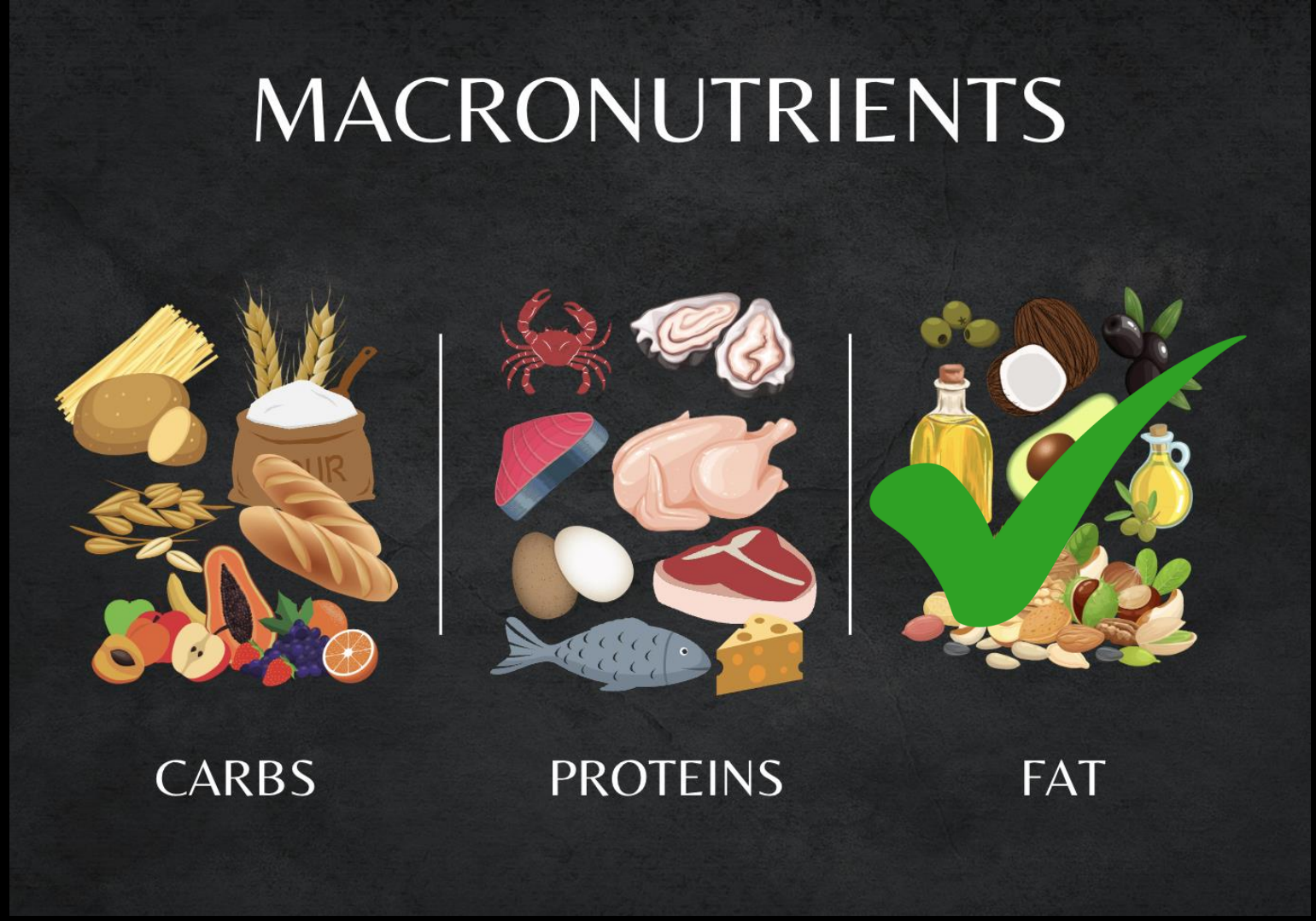
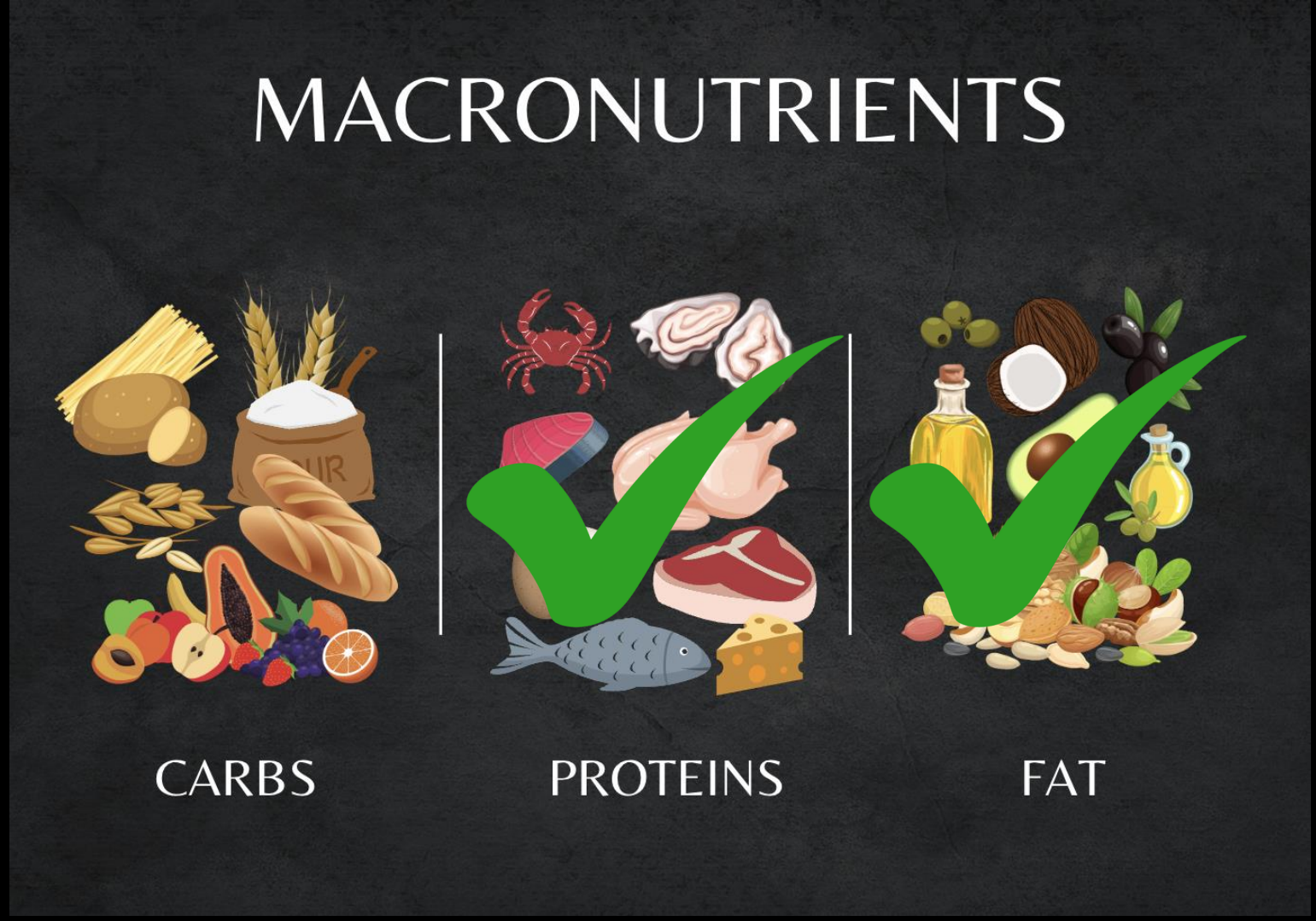


ESSENTIAL?



ESSENTIAL?



ESSENTIAL?







But surely we need glucose

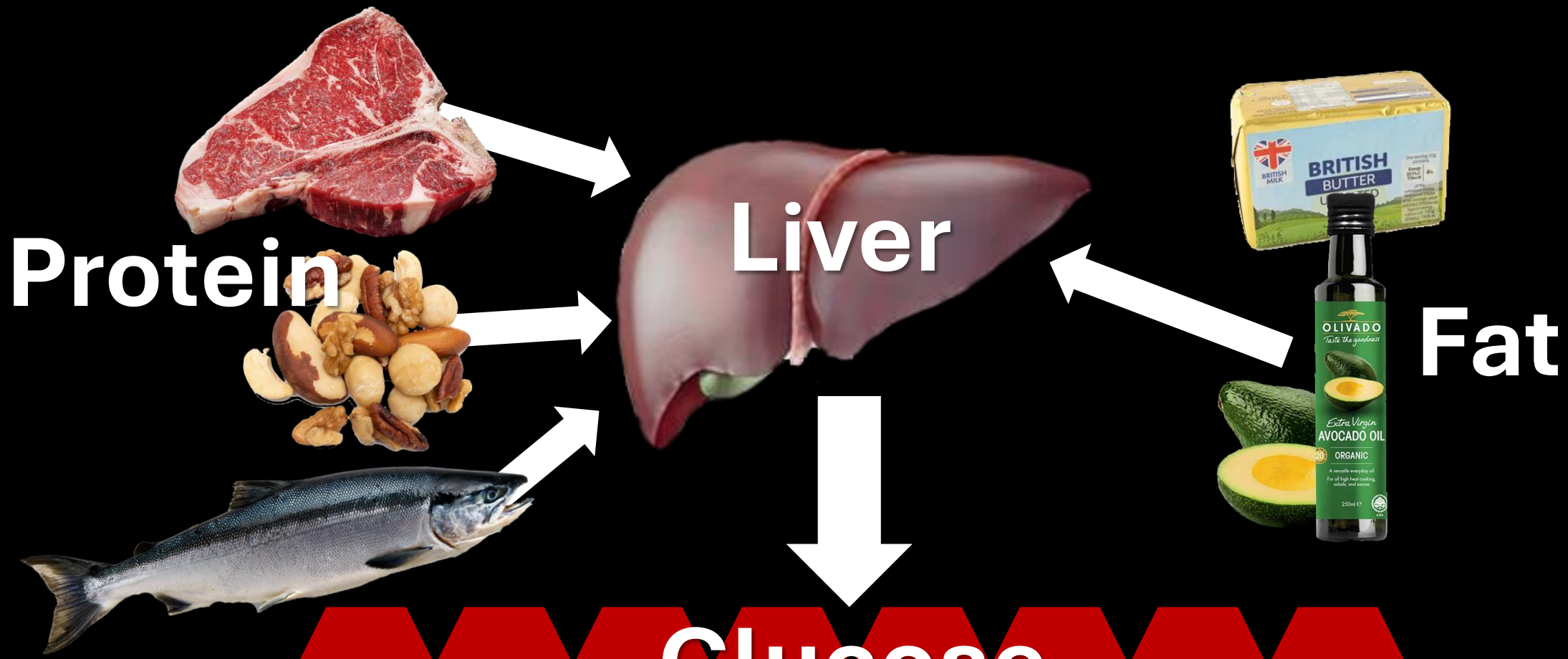
I was ~~learnt~~ taught it at school

ANY GLUCOSE WE DO NEED



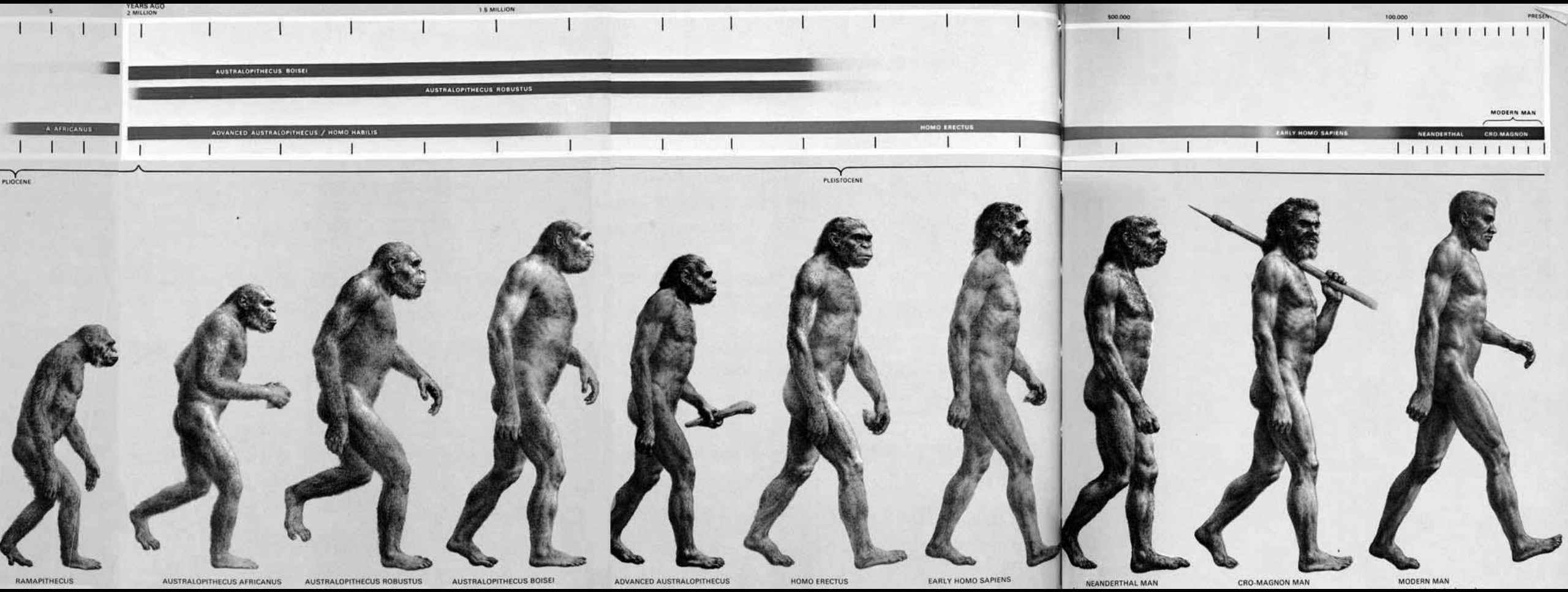
Glucose

ANY GLUCOSE WE DO NEED






Agricultural Revolution 12,000 – 5,000 BCE



2.5 million years

100,000 generations

Agricultural Revolution c. 8,000 BCE – 400 generations

10,000 years is not enough for us to have evolved to eat carbohydrates in large quantities


Bread

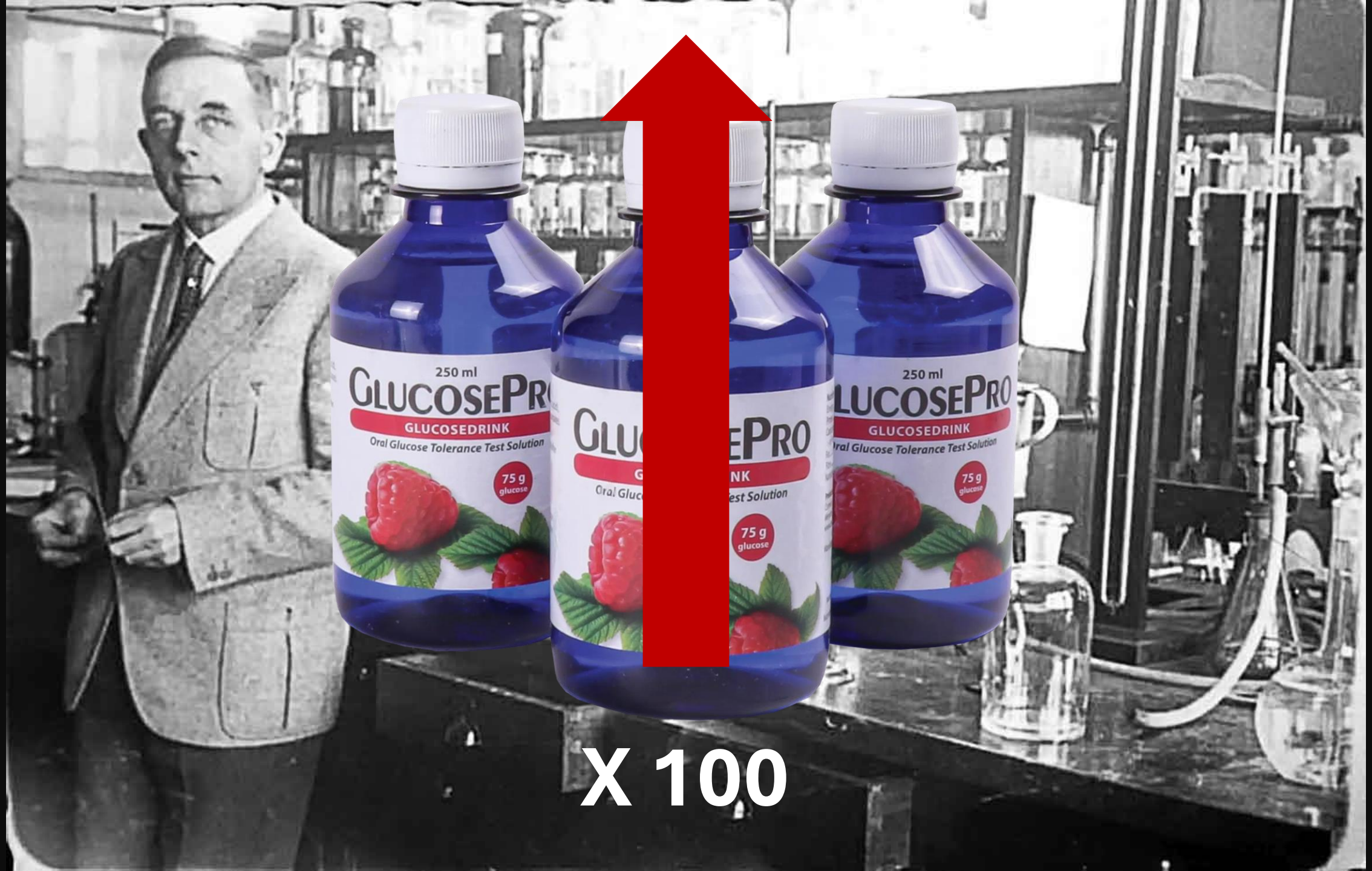

Cereal


Potatoes


Pizza


Pasta


Rice


250 ml
GLUCOSEDRINK
Oral Glucose Tolerance Test Solution
75 g
glucose
X 100

Eatwell Guide

Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.

Check the label on packaged foods

Each serving (150g) contains

Energy	Fat	Saturates	Sugars	Salt
1046kJ 250kcal	3.0g	1.3g	34g	0.9g
	LOW	LOW	HIGH	MED
13%	4%	7%	38%	15%

of an adult's reference intake

Typical values (as sold) per 100g: 697kJ/ 167kcal

Choose foods lower in fat, salt and sugars

Carbs



Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.



Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Choose lower fat and lower sugar options



Eat less often and in small amounts

Choose unsaturated oils and use in small amounts

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS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Each serving (150g) contains
Energy 1046kJ 250kcal 13%
Fat 3.0g LOW 4%
Saturates 1.3g LOW 7%
Sugars 34g HIGH 38%
Salt 0.9g MED 17%
of an adult's reference intake
Typical values (as sold) per 100g: 697kJ / 167kcal
Choose Foods lower in fat, salt and sugars
Crisps
sauce
Eat less often and in small amounts
Eat at least 5 portions of a variety of fruit and vegetables every day.
Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily
6-8 a day


THE EATWELL GUIDE
Adult
Calorie Intake Per Day
2000kcal
2500kcal
= All Food + All Drinks
Fruit and vegetables
5 per day
Potatoes, bread, rice, pasta and other starchy carbohydrates
Food and drinks high in sugar, fat and salt
Beans, pulses, fish 2 per week (1 oily and 1 not), eggs, meat and other proteins
Dairy and alternatives
Oil and spreads
Check the label on packaged foods
Choose foods lower in fat, salt and sugars
The Eatwell Guide
The Eatwell Guide Tabletop activity encourages students to think about the food they eat and the importance of eating a varied diet consisting of the right types and right amounts of food.
The activity could be used in different ways and includes pictures of a wide range of different food types.
The activity is relevant to the KS1 and KS2 programs of study in Science.


THE EATWELL GUIDE
Adult
Calorie Intake Per Day
2000kcal
2500kcal
= All Food + All Drinks
Fruit and vegetables
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Adult
Calorie Intake Per Day
2000kcal
2500kcal
= All Food + All Drinks
Eatwell Guide
The Nudge People
CAULIFLOWER
£1·20 each
ENGLAND
SAVOY CABBAGE
£1·20 each
ENGLAND
CABBAGE RED
£2.20 EACH
ENGLAND
Garlic
£0.40p
EACH
Scottish Eatwell Guide


Adult
Calorie Intake Per Day
2000kcal
2500kcal
= All Food + All Drinks
CAULIFLOWER
£1.20/ea
ENGLAND
Black Beans
SLICED CARROTS
BUTTER BEANS
RED KIDNEY BEANS
WHITE KIDNEY BEANS
Eatwell Guide: West Africans


Protecting and improving the nation's health
The Eatwell Guide
Helping you eat a healthy, balanced diet
Eatwell Guide
Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.
Water, lower fat milk, sugar-free drinks including tea and coffee all count.
Limit fruit juice and/or smoothies to a total of 150ml a day.
Potatoes, bread, rice, pasta and other starchy carbohydrates
Choose wholegrain or higher fibre versions with less added fat, salt and sugar
Oil & spreads
Choose unsaturated oils and use in small amounts
Dairy and alternatives
Choose lower fat and lower sugar options
Adult
Calorie Intake Per Day
2000kcal


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WRITING
KLIX
eatwell guide
Eatwell Guide: West African
FareShare
BUTTER BEANS
WHITE KIDNEY BEANS


Adult
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Potatoes, bread, rice, pasta
Water, lower fat milk, sugar-free drinks including tea and coffee
The South Asian Eatwell Guide
WeAreLPT
WRITING
KLIX
eatwell guide


Adult
Calorie Intake Per Day
2000kcal
eatwell guide
WRITING
Eatwell Guide
WHITE KIDNEY BEANS


Adult
Calorie Intake Per Day
2000kcal
Diabetes Specialist Nurses
Ulster Hospital: (028) 9056 1426
Ards Hospital: (028) 9181 8361
Bangor Hospital: (028) 9598 8082
Just Live a little
SUNFLOWER


Adult
Calorie Intake Per Day
2000kcal
Diabetes Specialist Nurses
Ulster Hospital: (028) 9056 1426
Ards Hospital: (028) 9181 8361
Bangor Hospital: (028) 9598 8082


Adult
Calorie Intake Per Day
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Diabetes Specialist Nurses
Ulster Hospital: (028) 9056 1426
Ards Hospital: (028) 9181 8361
Bangor Hospital: (028) 9598 8082
Vegan Eatwell Guide


Adult
Calorie Intake Per Day
2000kcal
Diabetes Specialist Nurses
Ulster Hospital: (028) 9056 1426
Ards Hospital: (028) 9181 8361
Bangor Hospital: (028) 9598 8082
The Eatwell Plate
Carbohydrates
Fruit and Vegetables
Milk and Dairy
Fish, Eggs, meat, beans
Fats and Sugars
Oatibix
ALPHA BITES

“Exceedingly unusual behaviour”

Nick Crawford, The Metabolic Approach, 2026.

Eatwell Guide

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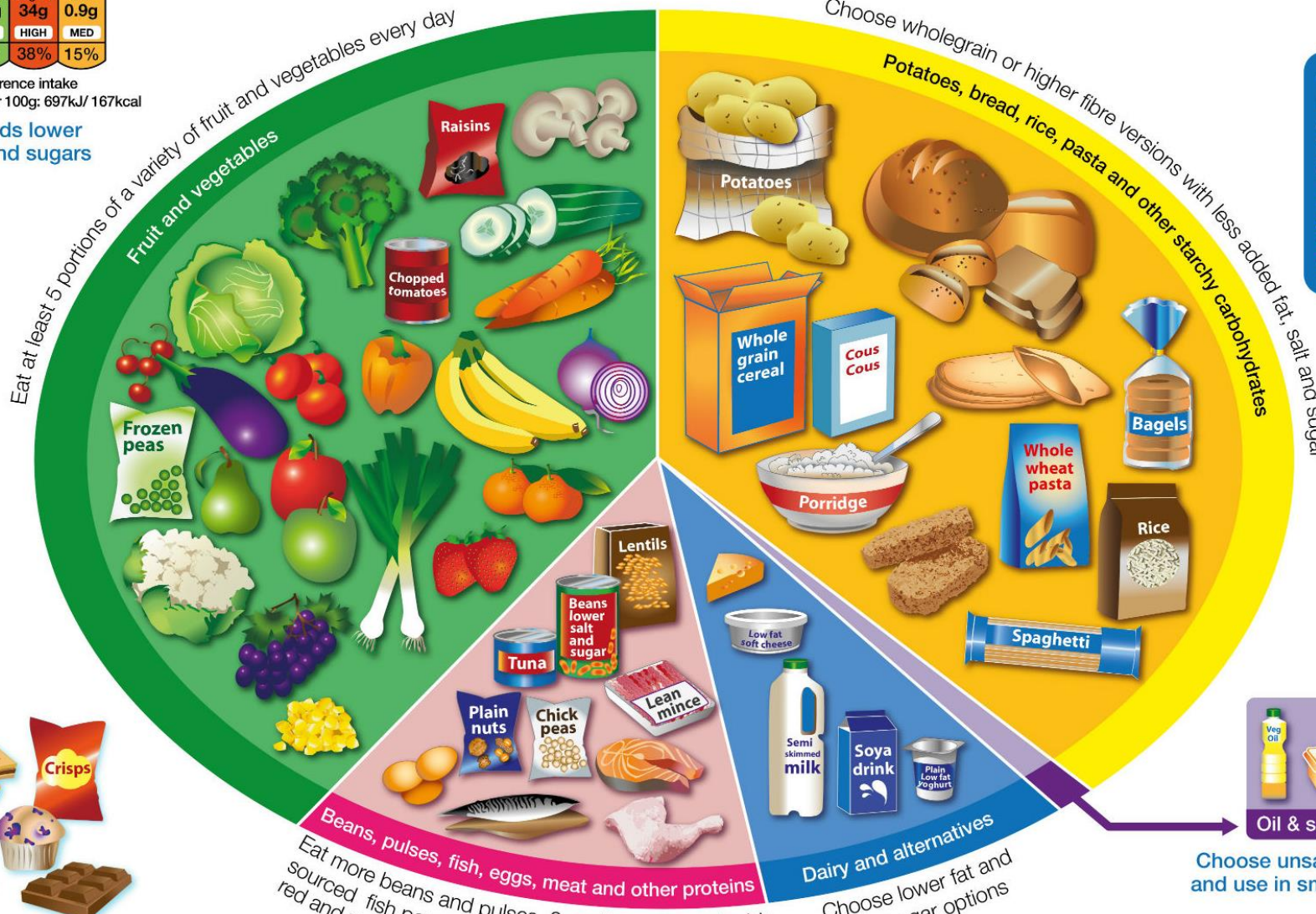

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Department of Health

Report on Health and Social Subjects

41

Dietary Reference Values for Food Energy and Nutrients for the United Kingdom

Report of the Panel on Dietary Reference Values
of the Committee on Medical Aspects of Food Policy

TSO

Table 1.2 *Dietary Reference Values for fat and carbohydrate for adults as a percentage of daily total energy intake (percentage of food energy)*

	Individual minimum	Population average	Individual maximum
Saturated fatty acids		10 (11)	
Cis-polyunsaturated fatty acids		6 (6.5)	10
	n−3 0.2		
	n−6 1.0		
Cis-monounsaturated fatty acids		12 (13)	
Trans fatty acids		2 (2)	
Total fatty acids		30 (32.5)	
TOTAL FAT		33 (35)	
Non-milk extrinsic sugars	0	10 (11)	
Intrinsic and milk sugars and starch		37 (39)	
TOTAL CARBOHYDRATE		47 (50)	
NON-STARCH POLYSACCHARIDE (g/d)	12	18	24

FAT

CARBS

PROTEIN

The average percentage contribution to total energy doe[illegible]otal 100% because figures for protein and alcohol are excluded. Protein intakes average 15 per cent of total energy which is above the RNI. It is recognised that many individuals will derive some energy from alcohol, and this has been assumed to average 5 per cent approximating to current intakes. However the Panel allowed that some groups might not drink alcohol and that for some purposes nutrient intakes as a proportion of food energy (without alcohol) might be useful. Therefore average figures are given as percentages both of total energy and, in parenthesis, of food energy.

UK, and should not be taken to represent 'ideal' figures.

1.3.6 The information from which estimates of requirements have been made can be categorised as follows:

a. the intakes of a nutrient needed to maintain a given circulating level or degree of enzyme saturation or tissue concentration;

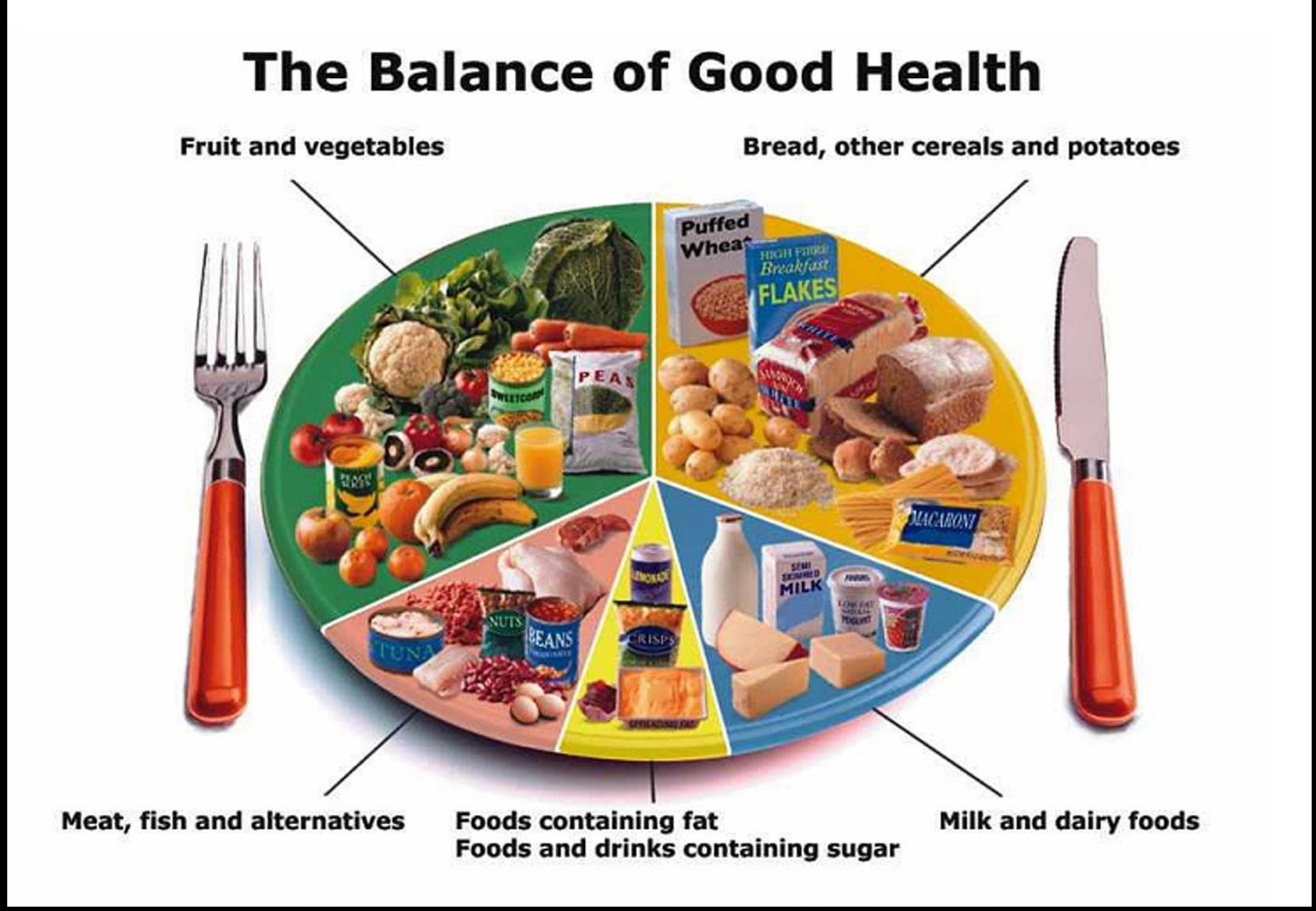
b. the intakes of a nutrient by individuals and by groups which are associated with the absence of any signs of deficiency diseases;

c. the intakes of a nutrient needed to maintain balance noting that the period over which such balance needs to be measured differs for different nutrients, and between individuals;

d. the intakes of a nutrient needed to cure clinical signs of deficiency;

e. the intakes of a nutrient associated with an appropriate biological marker of nutritional adequacy.

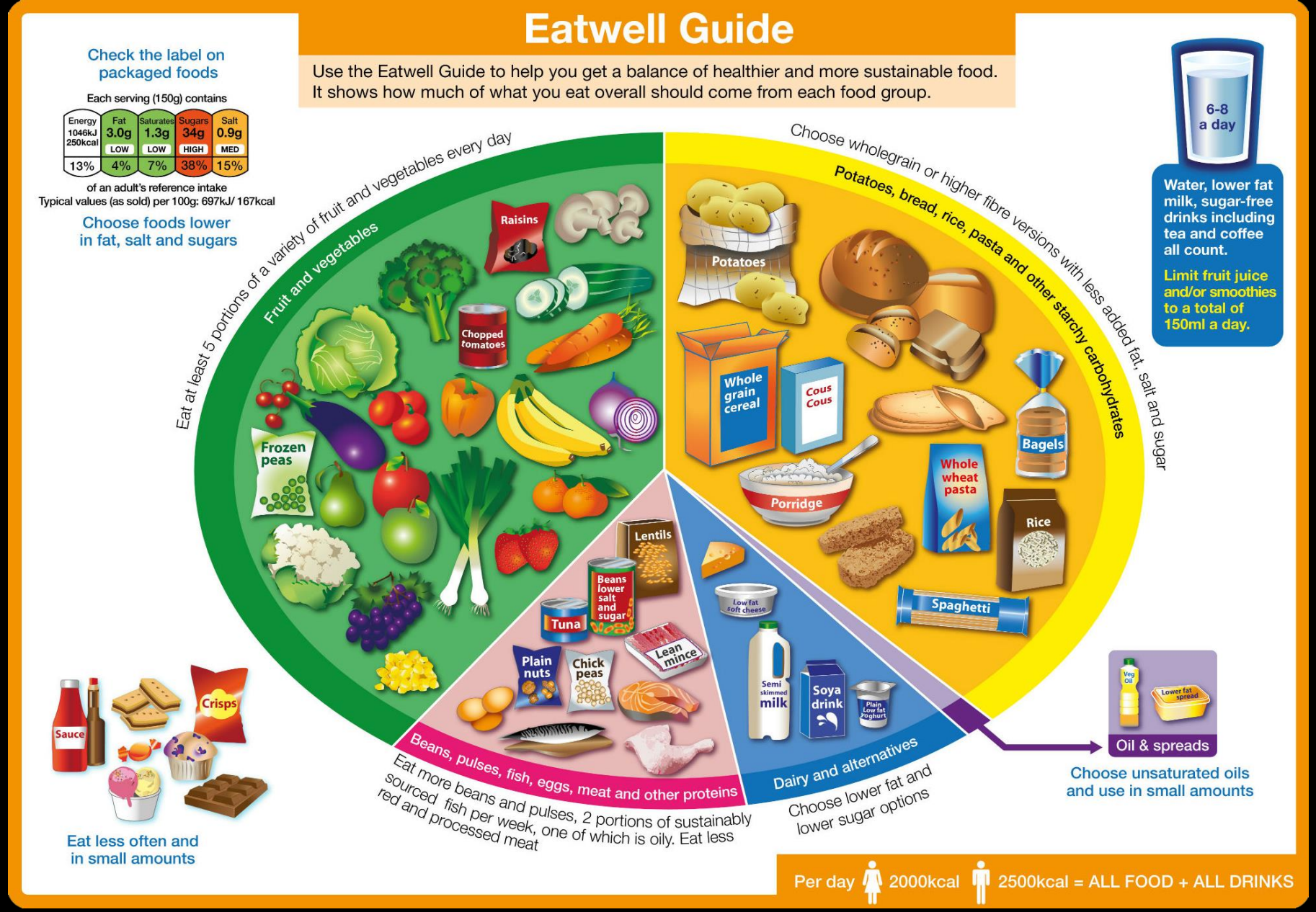
1.3.7 The Panel found no single criterion to define requirements for all nutrients. Some nutrients may have a variety of physiological effects at different levels of intake. Which of these effects should form the parameter of adequacy is therefore to some extent arbitrary. For each nutrient the particular parameter or parameters which were used to define adequacy are given in the text. None of these criteria is perfect, but they were judged to be the best available on which to base DRV so that they were relevant to prevailing circumstances. In some cases the evidence on which they are based is reliable



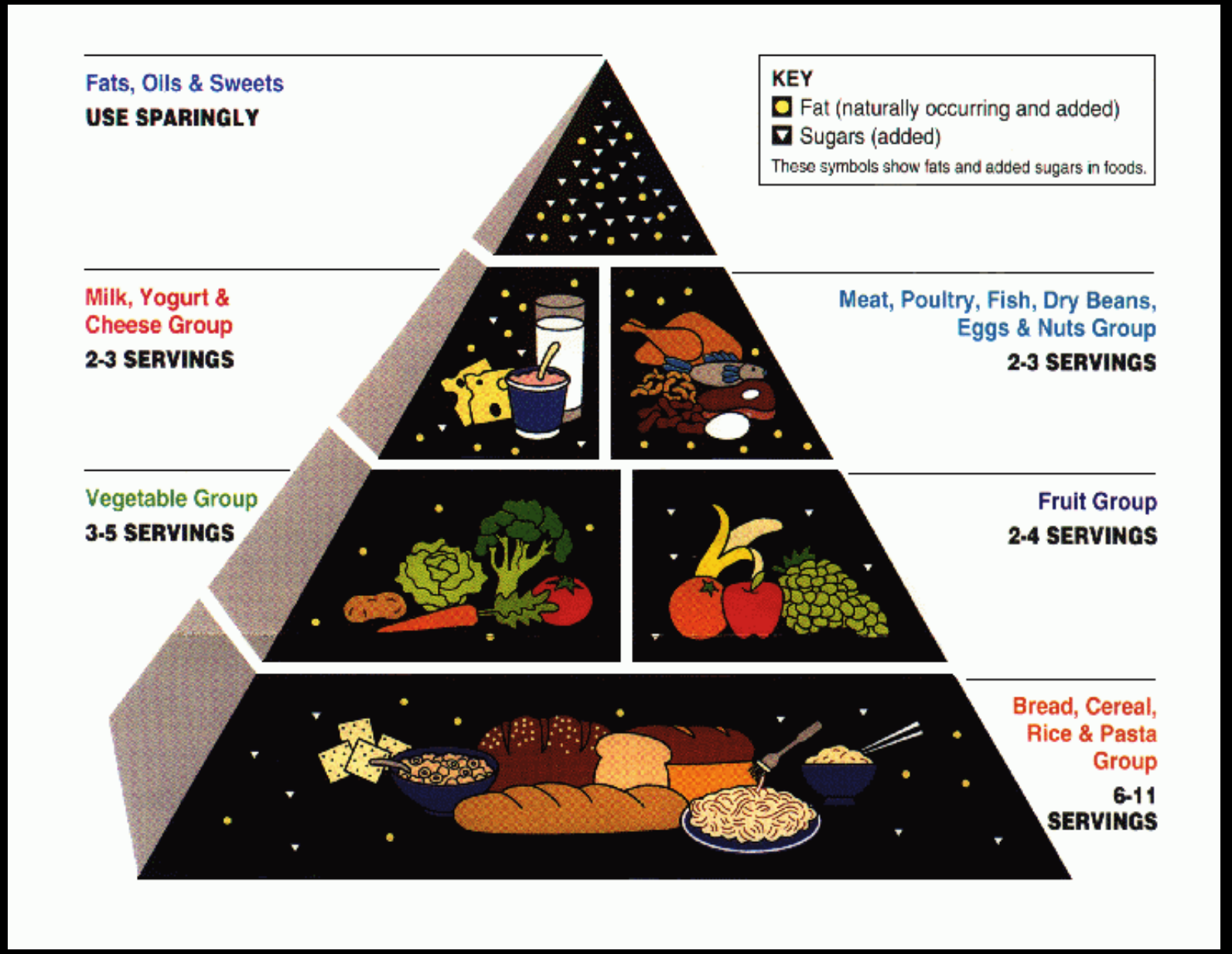
The Balance of Good Health, 1994



The Eatwell Plate, 2007



The Eatwell Guide, 2016



US MyPyramid, 2005 - 2011

Heart Disease and Stroke Statistics—2015 Update

A Report From the American Heart Association

WRITING GROUP MEMBERS

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ls.org by on September 25, 2026

on cardiovascular health by considering only a limited number of pathways (eg, only effects on lipids, BP, and obesity) will systematically underestimate or even misconstrue the actual total impact on cardiovascular health. Randomized controlled trials and prospective observational studies have been used to quantify the total effects of dietary habits on clinical outcomes.

Fats and Carbohydrates

- In the WHI randomized clinical trial (n=48 835), reduction of total fat consumption from 37.8% energy (baseline) to 24.3% energy (at 1 year) and 28.8% energy (at 6 years) had no effect on incidence of CHD (RR, 0.98; 95% CI, 0.88–1.09), stroke (RR, 1.02; 95% CI, 0.90–1.15), or total CVD (RR, 0.98; 95% CI, 0.92–1.05) over a mean of 8.1 years.[75] This was consistent with null results of 4 prior randomized clinical trials and multiple large prospective cohort studies that indicated little effect of total fat consumption on CVD risk.[76]
- In 3 separate meta-analyses of prospective cohort studies, the largest of which included 21 studies with up to 2 decades of follow-up, saturated fat consumption overall had no significant association with incidence of CHD, stroke, or total CVD.[77–79] In comparison, in a pooled individual-level analysis of 11 prospective cohort studies, the specific exchange of polyunsaturated fat consumption in place of saturated fat was associated with lower CHD risk, with 13% lower risk for each 5% energy exchange (RR, 0.87; 95% CI, 0.70–0.97).[80] These findings are consistent with a meta-analysis of randomized controlled trials in which increased polyunsaturated fat consumption in place of saturated fat reduced CHD events, with 10% lower risk for each 5% energy exchange (RR, 0.90; 95% CI, 0.83–0.97).[81]
- In meta-analyses of prospective cohort studies, each daily serving of fruits or vegetables was associated with a 4% lower risk of CHD (RR, 0.96; 95% CI, 0.93–0.99) and a 5% lower risk of stroke (RR, 0.95; 95% CI, 0.92–0.97).[85,86]
- In a meta-analysis of prospective cohort studies, greater whole grain intake (2.5 compared with 0.2 servings per day) was associated with a 21% lower risk of CVD events (RR, 0.79; 95% CI, 0.73–0.85), with similar estimates in men and women and for various outcomes (CHD, stroke, and fatal CVD). In contrast, refined grain intake was not associated with lower risk of CVD (RR, 1.07; 95% CI, 0.94–1.22).[87]
- In a meta-analysis of 16 prospective cohort studies that included 326 572 generally healthy individuals in Europe, the United States, China, and Japan, fish consumption was associated with significantly lower risk of CHD mortality.[88] Compared with no consumption, an estimated 250 mg of long-chain omega-3 fatty acids per day was associated with 35% lower risk of CHD death ($P<0.001$).
- In a meta-analysis of prospective cohort and case-control studies from multiple countries, consumption of unprocessed red meat was not significantly associated with incidence of CHD. In contrast, each 50-g serving per day of processed meats (eg, sausage, bacon, hot dogs, deli meats) was associated with a higher incidence of CHD (RR, 1.42; 95% CI, 1.07–1.89).[89]
- In a meta-analysis of prospective cohort studies that included 442 101 participants and 28 228 DM cases, unprocessed red meat consumption was associated with a higher risk of DM (RR, 1.19; 95% CI, 1.04–1.37, per 100 g/d). On a per g/d basis, risk of DM was nearly 7-fold higher for processed meat consumption (RR, 1.51; 95% CI, 1.25–1.83, per 50 g/d).[90]

- A review of cross-sectional and prospective cohort studies suggests that higher intake of sugar-sweetened beverages is associated with greater visceral fat and higher risk of type 2 DM.[71]
- In a randomized controlled trial, compared with a low-fat diet, 2 Mediterranean dietary patterns that included either virgin olive oil or mixed nuts lowered SBP by 5.9 and 7.1 mm Hg, plasma glucose by 7.0 and 5.4 mg/dL, fasting insulin by 16.7 and 20.4 pmol/L, the homeostasis model assessment index by 0.9 and 1.1, and the ratio of total to HDL cholesterol by 0.38 and 0.26 and raised HDL cholesterol by 2.9 and 1.6 mg/dL, respectively. The Mediterranean dietary patterns also lowered levels of CRP, interleukin-6, intercellular adhesion molecule-1, and vascular cell adhesion molecule-1.[72]
- Among 24 prospective cohort studies, greater consumption of refined carbohydrates and sugars, as measured by higher glycemic load, was positively associated with risk of type 2 DM: for each 100-g increment, 45% higher risk was seen (95% CI, 1.31–1.61) for a 100-g increment in glycemic load ($P<0.001$; n=24 studies, 7.5 million person-years of follow-up).[73]
- In one meta-analysis of observational studies and trials, greater consumption of nuts was linked to lower incidence of type 2 DM (RR per 4 weekly 1-oz servings, 0.87; 95% CI, 0.81–0.94).[74]

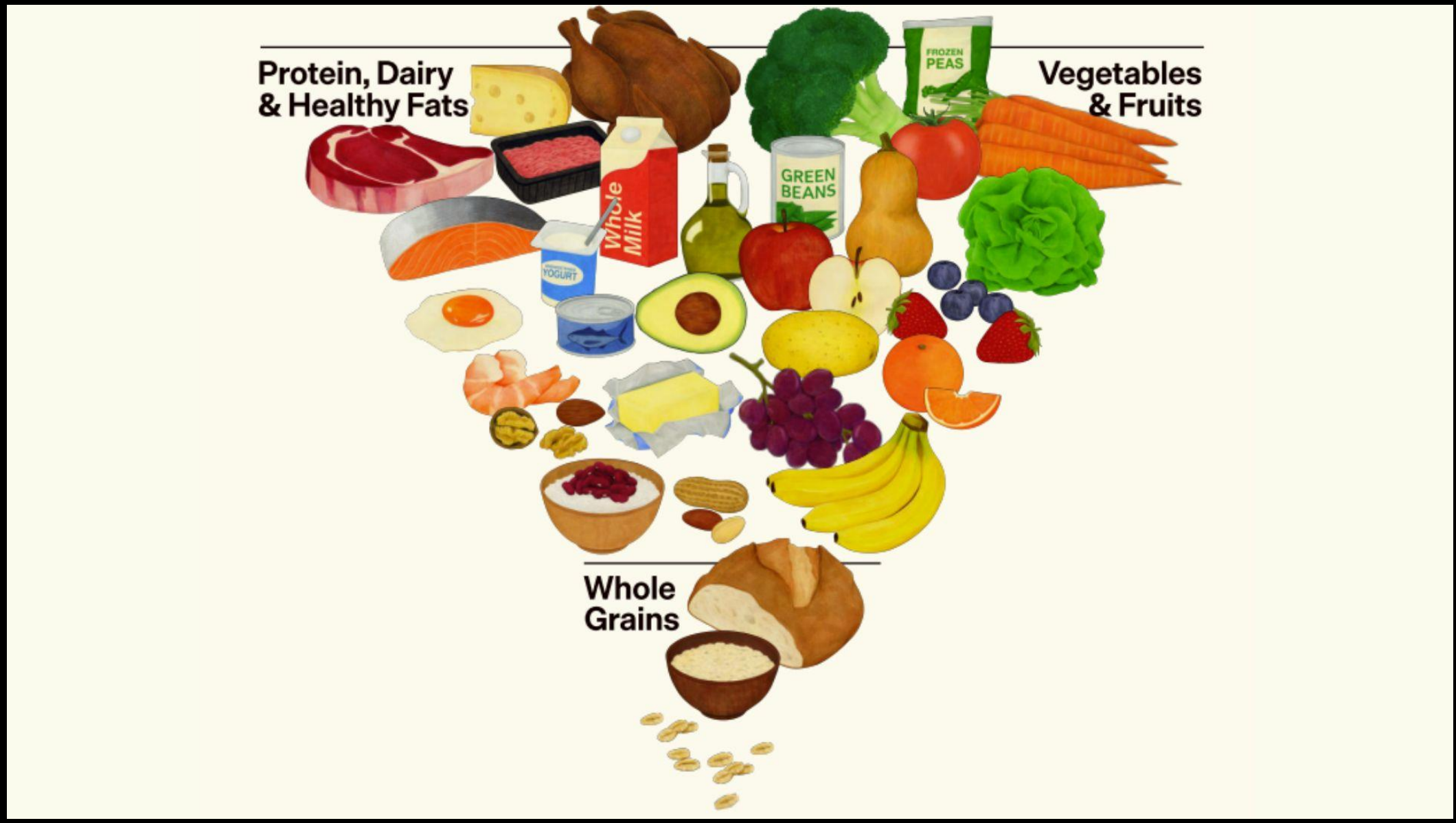
Effects on Cardiovascular Outcomes

Because dietary habits affect a broad range of established and novel risk factors, estimation of the impact of nutritional factors

- In a pooled analysis of individual-level data from 11 prospective cohort studies in the United States, Europe, and Israel that included 344 696 participants, each 5% higher energy consumption of carbohydrate in place of saturated fat was associated with a 7% higher risk of CHD (RR, 1.07; 95% CI, 1.01–1.14).[80] Each 5% higher energy consumption of monounsaturated fat in place of saturated fat was not significantly associated with CHD risk.[80] A more recent meta-analysis of prospective cohort studies found that increased intake of polyunsaturated fats was associated with lower risk of CHD, whether replacing saturated fat or carbohydrate.[80a]
- Together these findings suggest that reducing saturated fat without specifying the replacement may have minimal effects on CHD risk, whereas increasing polyunsaturated fats from vegetable oils will reduce CHD, whether replacing saturated fat or carbohydrate.[1]
- In a meta-analysis of prospective cohort studies, each 2% of calories from *trans* fat was associated with a 23% higher risk of CHD (RR, 1.23; 95% CI, 1.11–1.37).[82]
- In meta-analyses of prospective cohort studies, greater consumption of refined complex carbohydrates, starches, and sugars, as assessed by glycemic index or load, was associated with significantly higher risk of CHD and DM. When the highest category was compared with the lowest category, risk of CHD was 36% greater (glycemic load: RR, 1.36; 95% CI, 1.13–1.63), and risk of DM was 40% greater (glycemic index: RR, 1.40; 95% CI, 1.23–1.59).[83,84]

Foods and Beverages

Downloaded from http://ahajourn



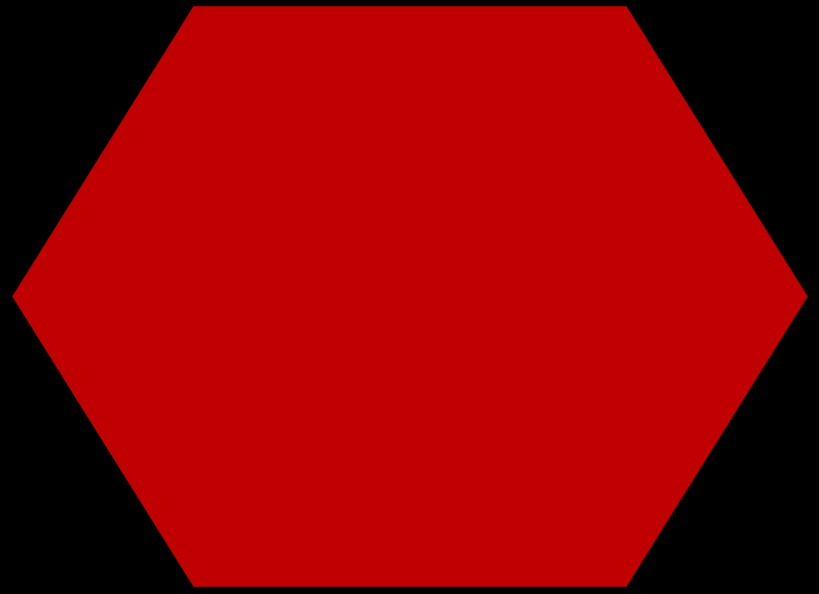
US Inverted Pyramid, 2026

SANITY CHECK 2

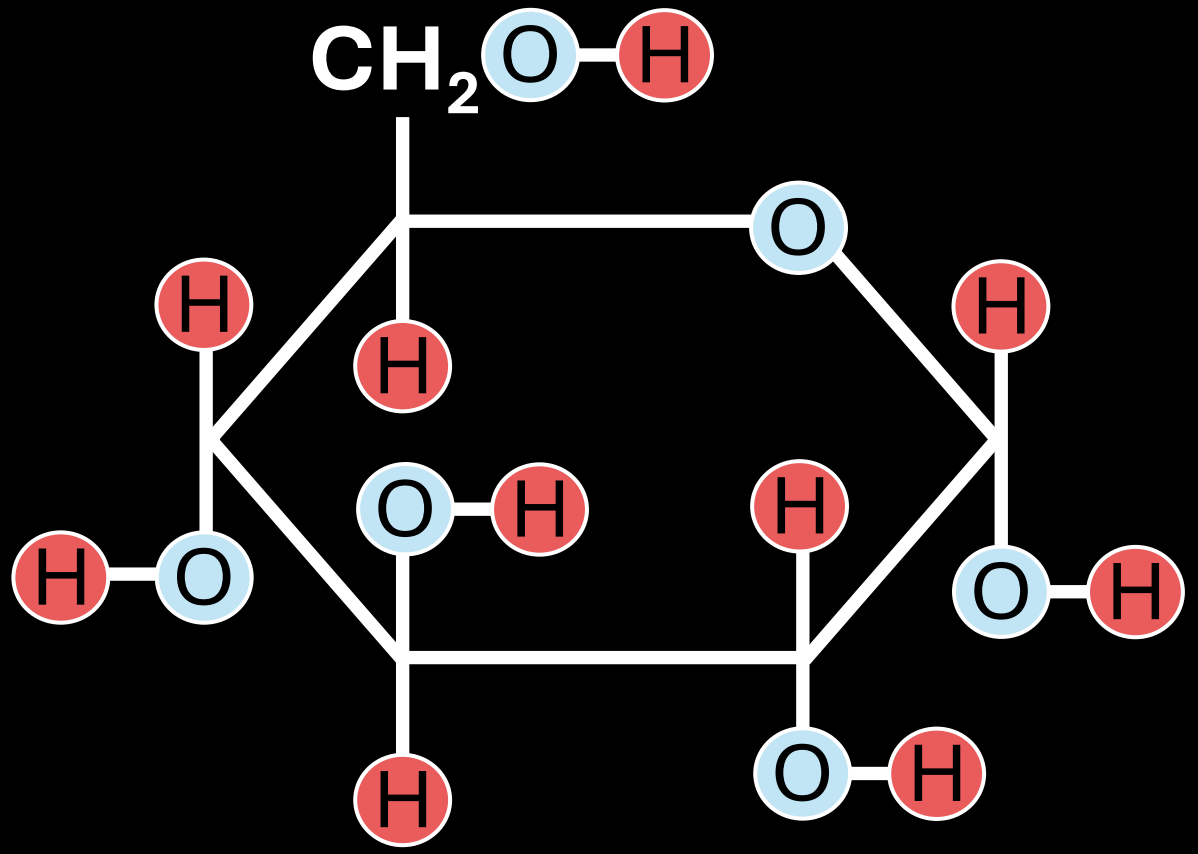
Modern medicine already makes use of cancer’s love of glucose!



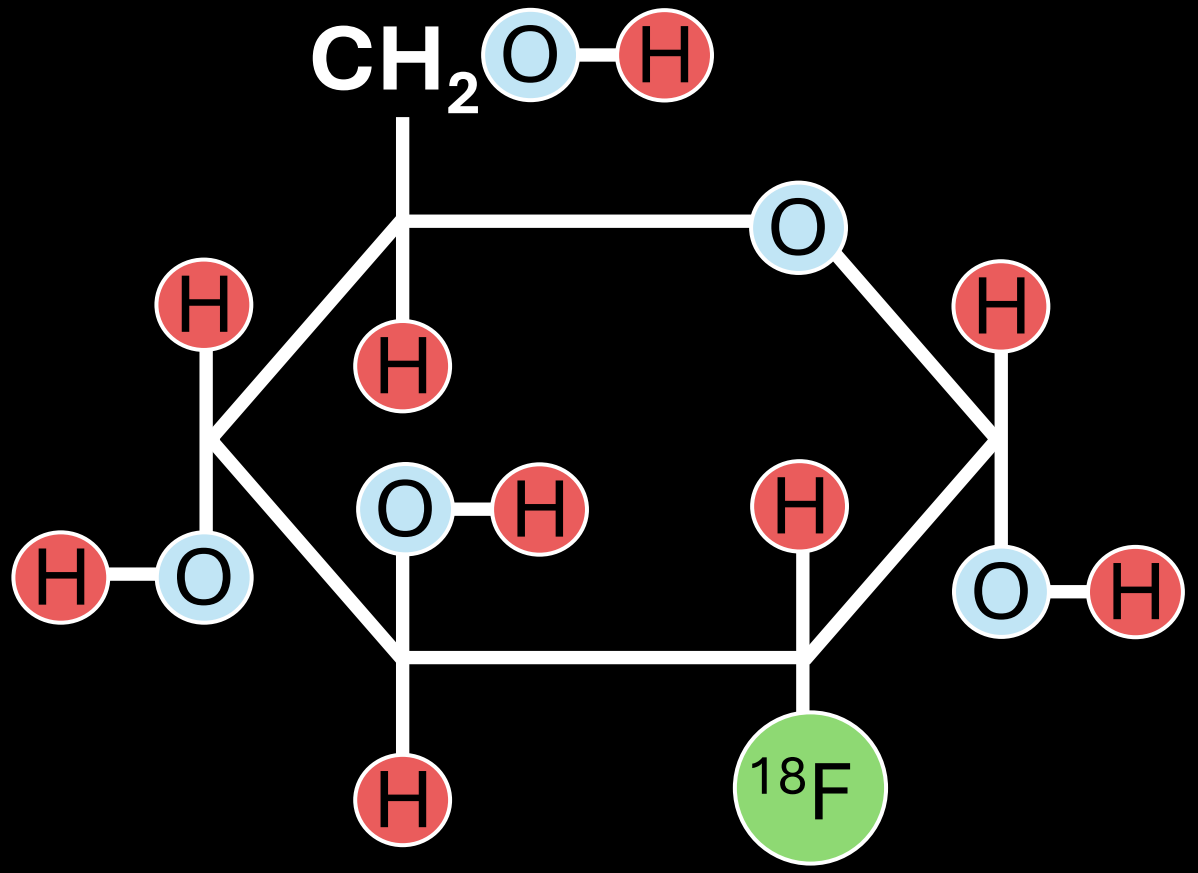
PET Scanner



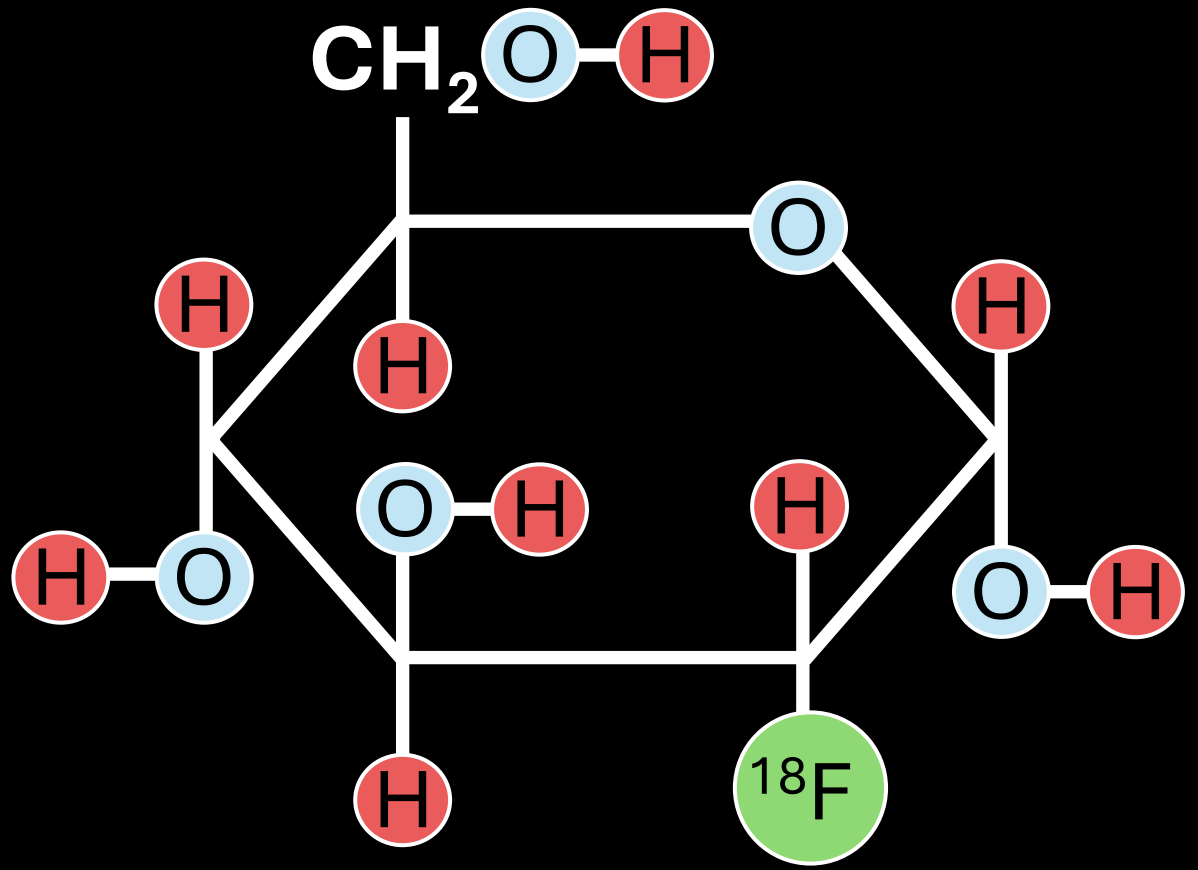
Glucose



Glucose



Fluorodeoxyglucose

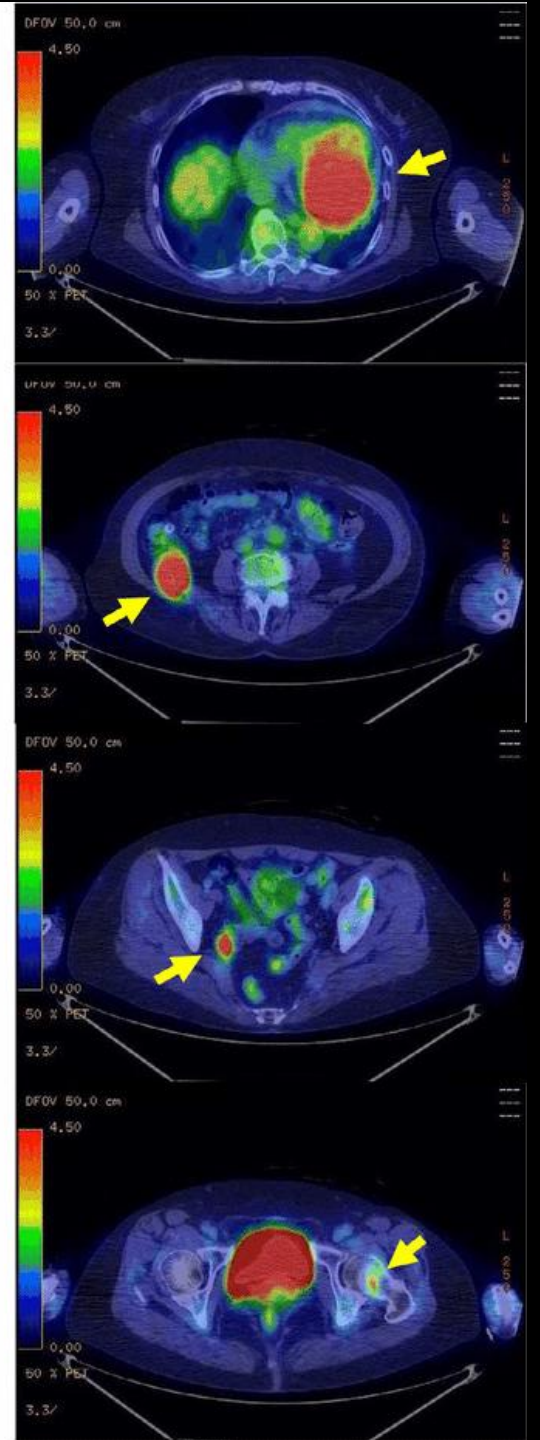


Fluorodeoxyglucose



PET Scan Glucose Injection





SANITY CHECK 2

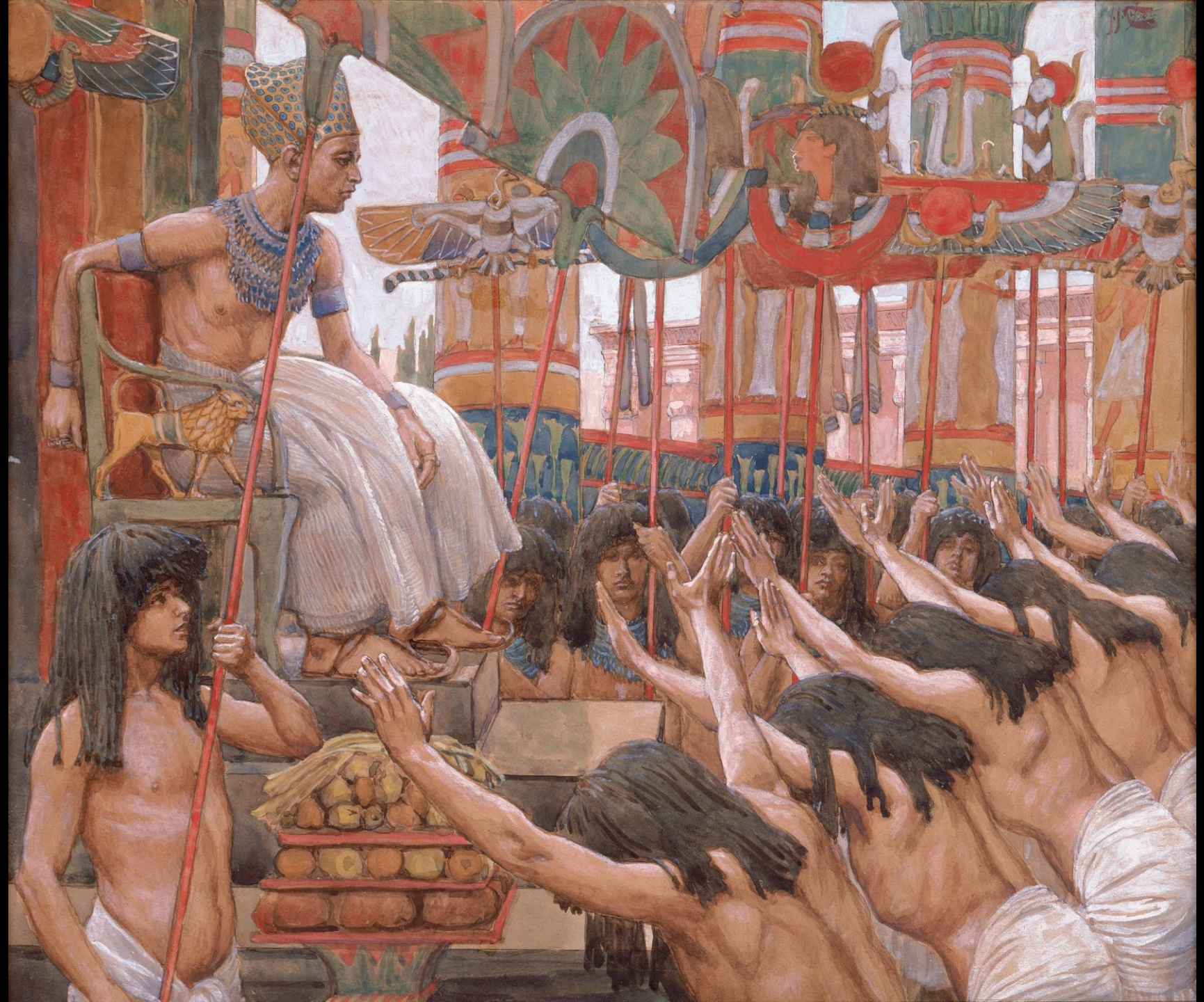
‘The images produced by a PET scan are a dramatic visualisation of cancer’s grotesquely voracious appetite for glucose.’

Tripping Over the Truth – Travis Christofferson

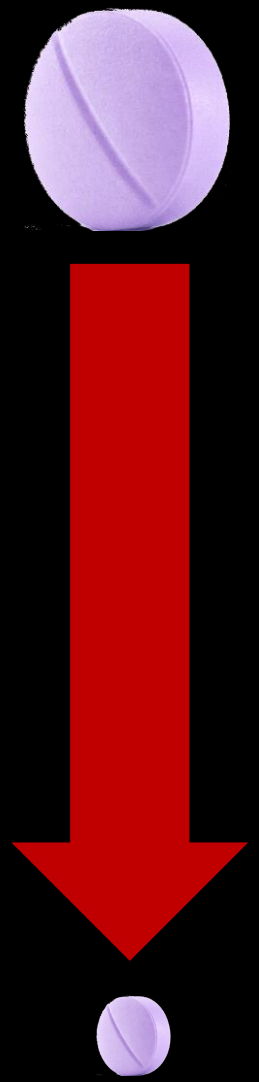

INTERMISSION


Star
of the
SHOW

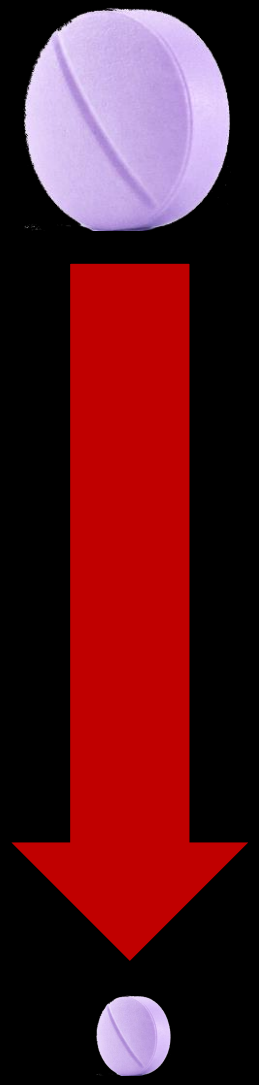
KETONES



GLUCOSE & GLYCOGEN



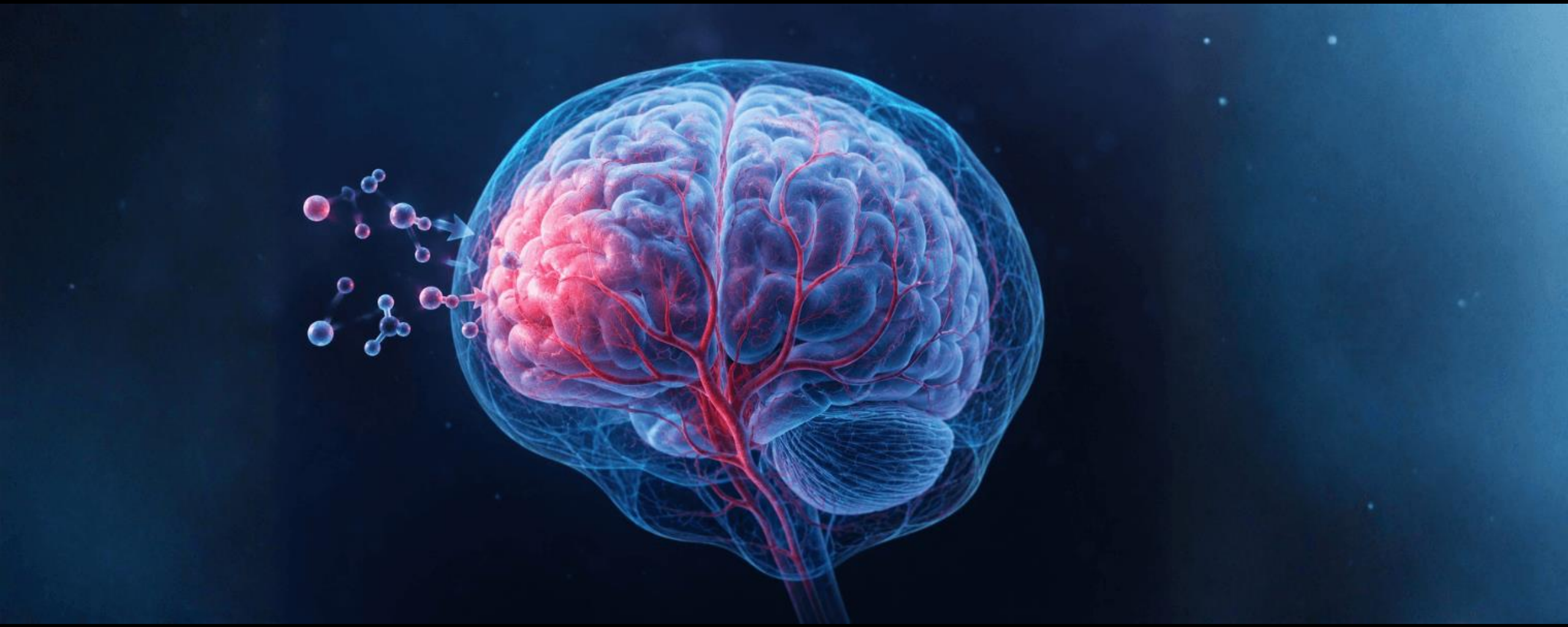
GLUCOSE & GLYCOGEN



STORED FAT



BLOOD BRAIN BARRIER



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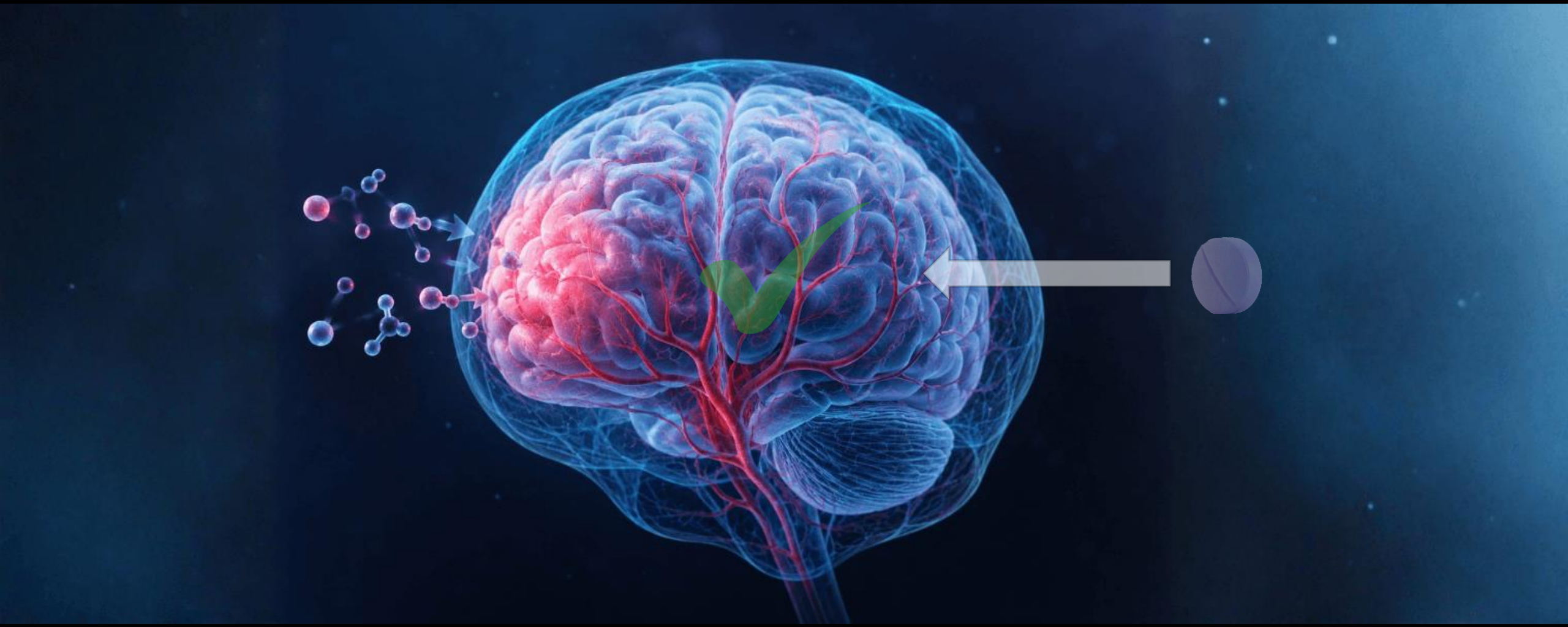


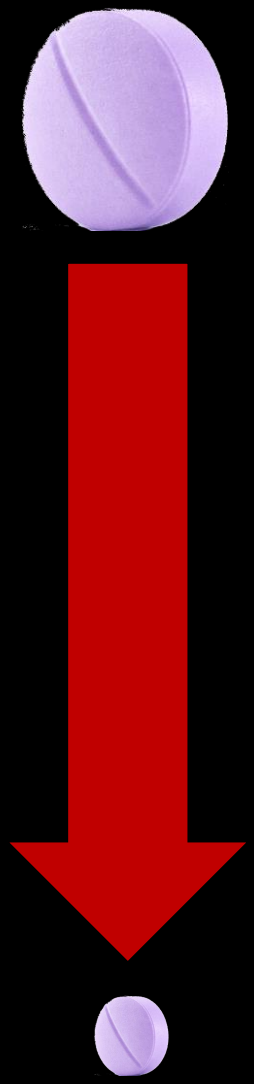
BLOOD BRAIN BARRIER



BLOOD BRAIN BARRIER



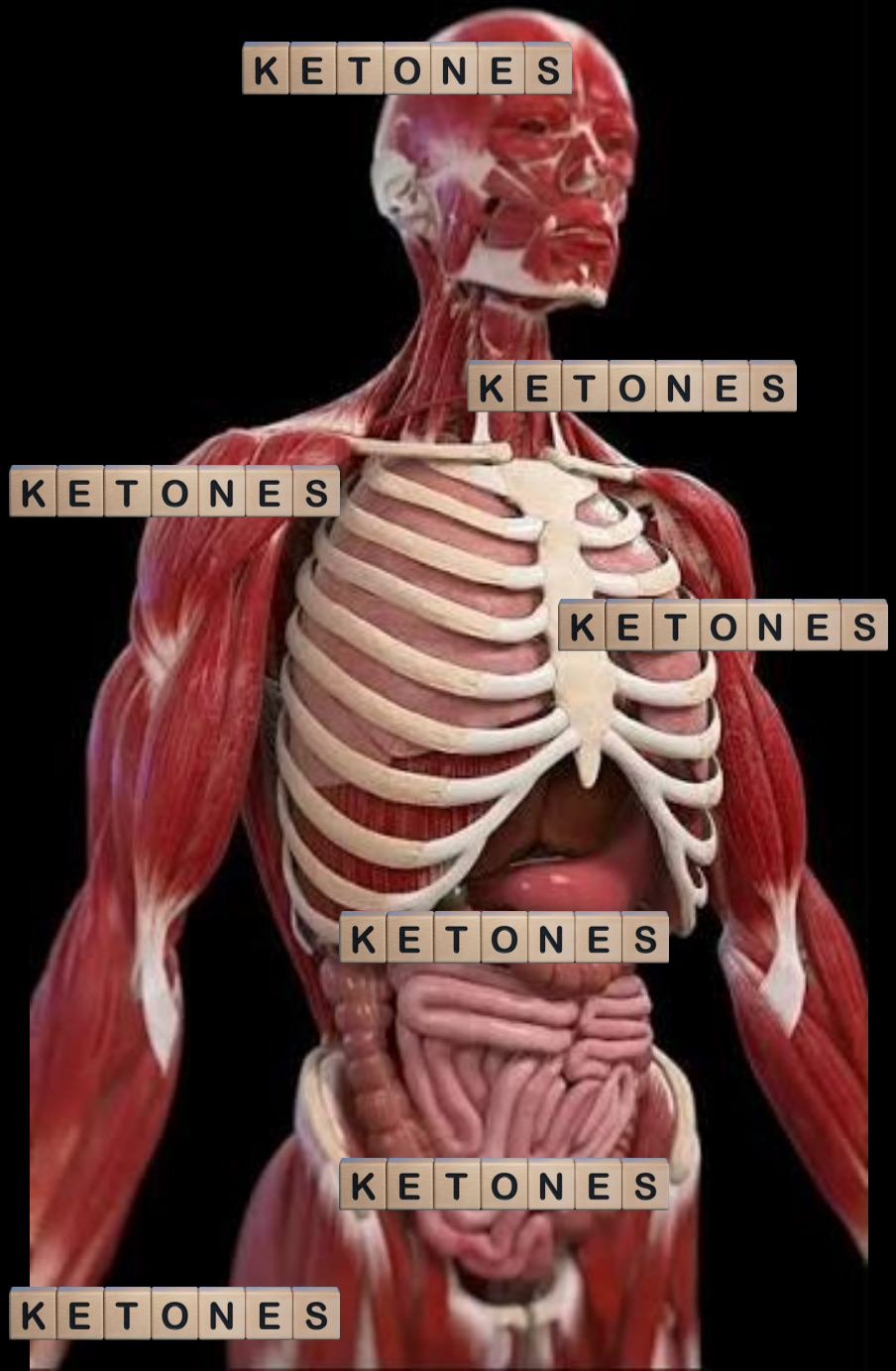
GLUCOSE & GLYCOGEN





BLOOD BRAIN BARRIER

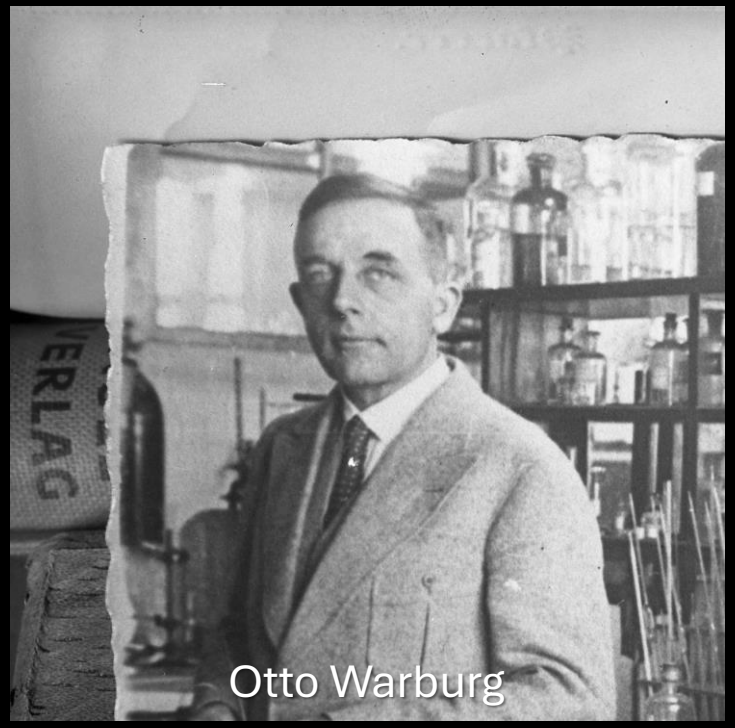



KETONES
KETONES
KETONES
KETONES
KETONES
KETONES
KETONES



ENERGY

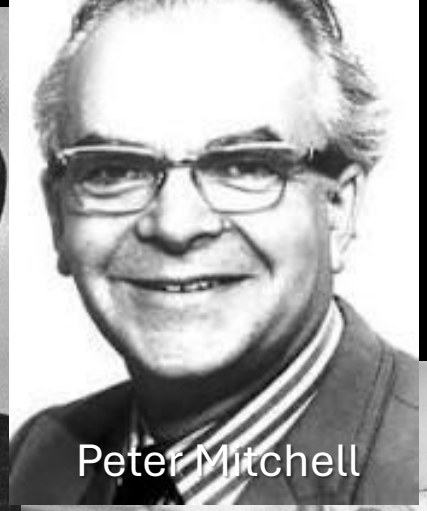
METABOLISM



What Warburg didn’t know…
…that we do now:



Hans Adolf Krebs



Peter Mitchell





Albert Szent-Gy



Eugene Kennedy

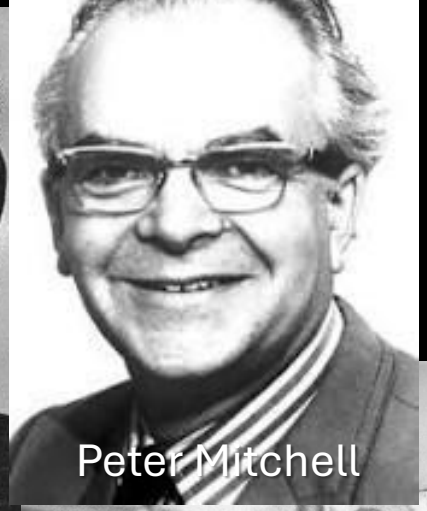


Albert Lehninger

What Warburg didn't know...
...that we do now:



Hans Adolf Krebs



Peter Mitchell





Albert Szent-Gy



Eugene Kennedy

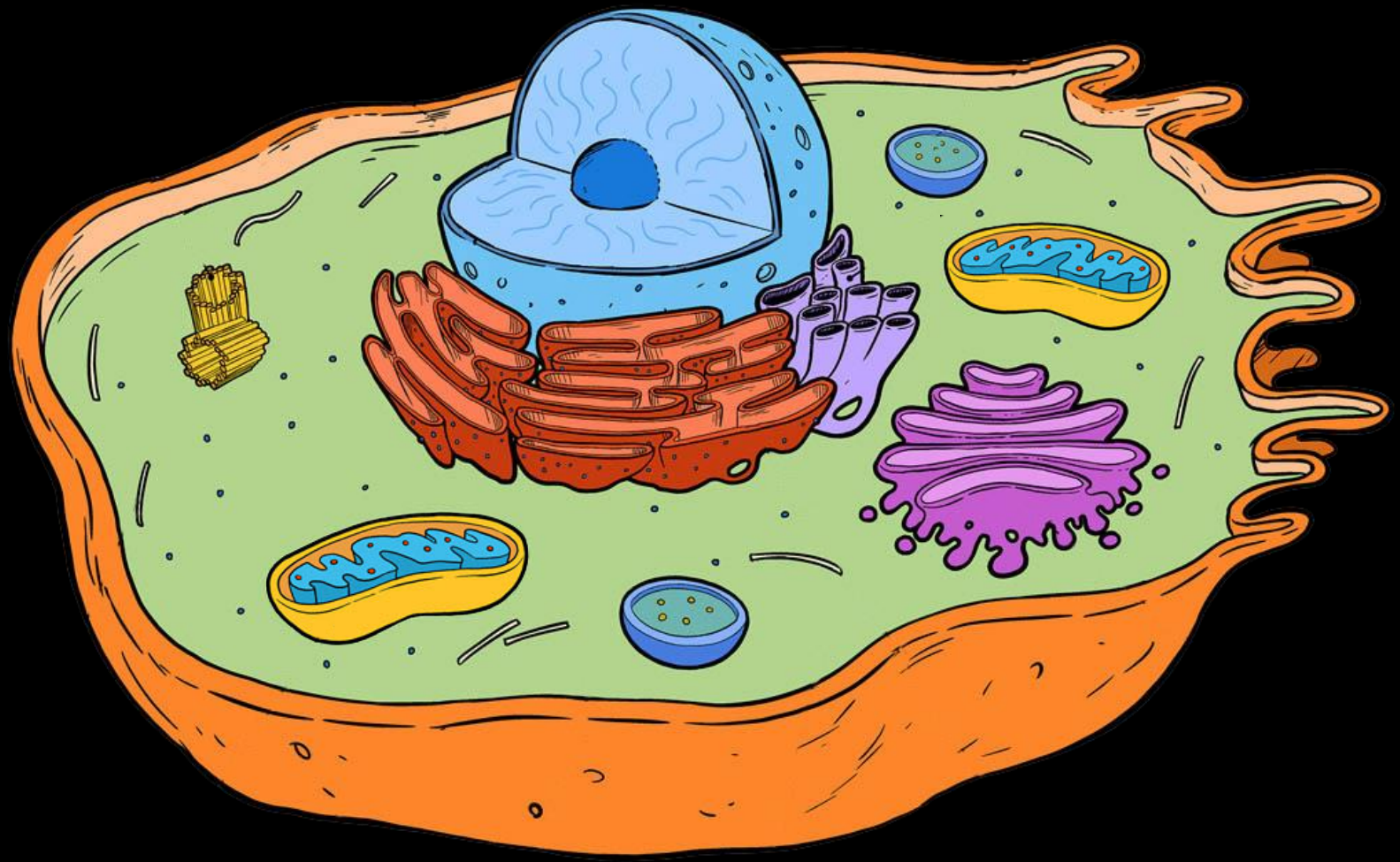


Albert Lehninger

What Warburg didn't know...
...that we do now:

Mitochondria









MITOCHONDRIA

The powerhouse of the cell

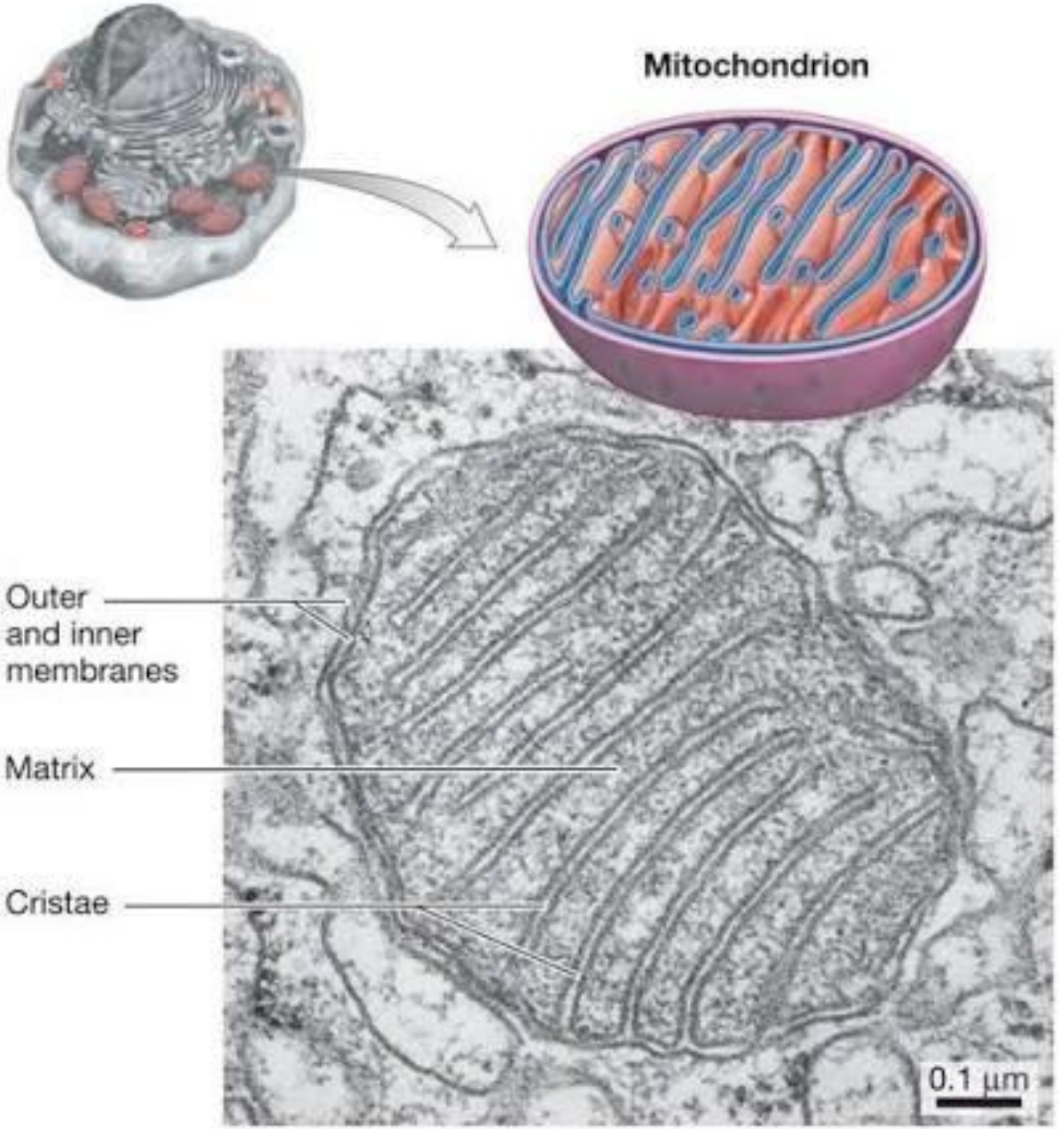


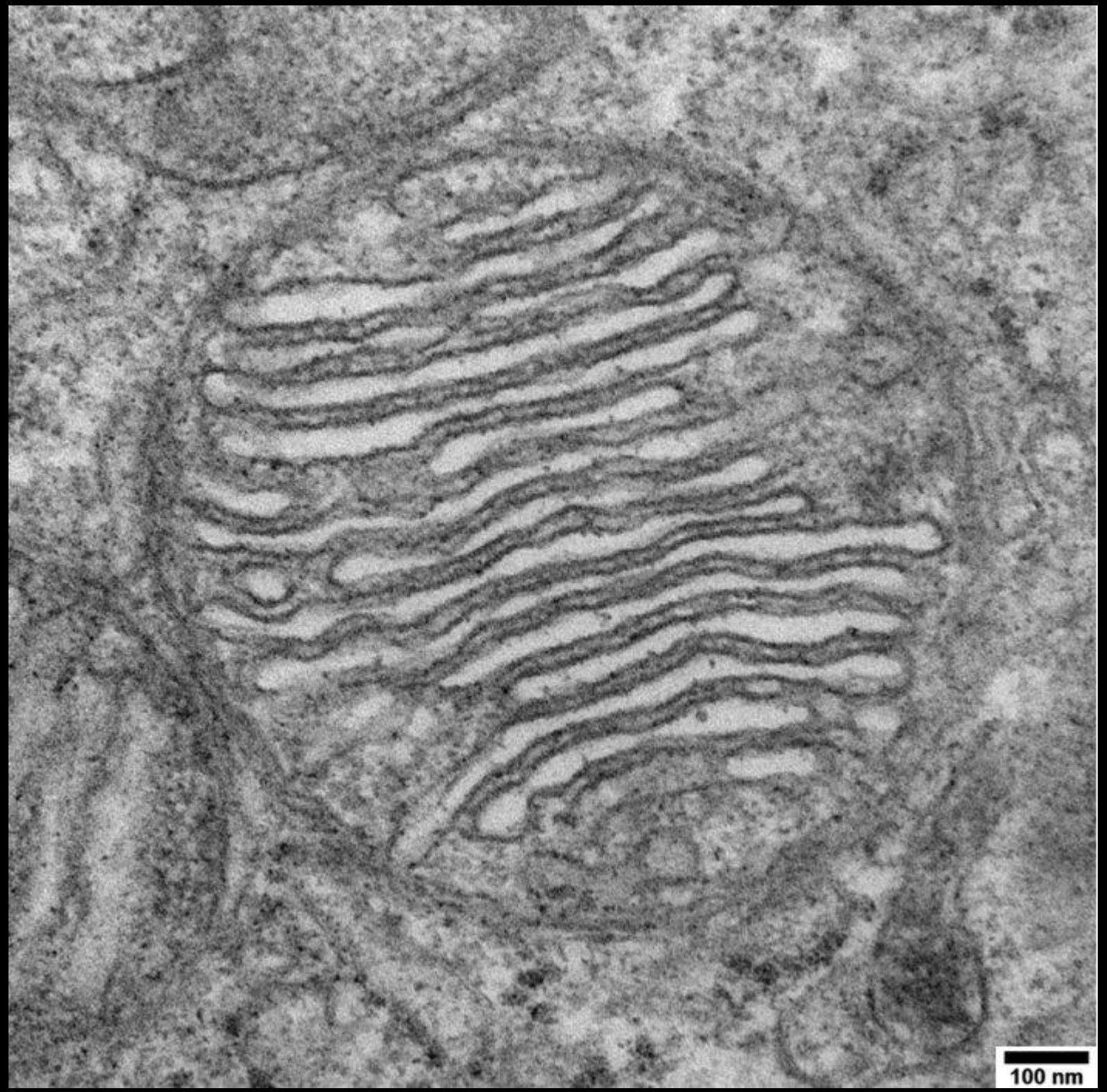


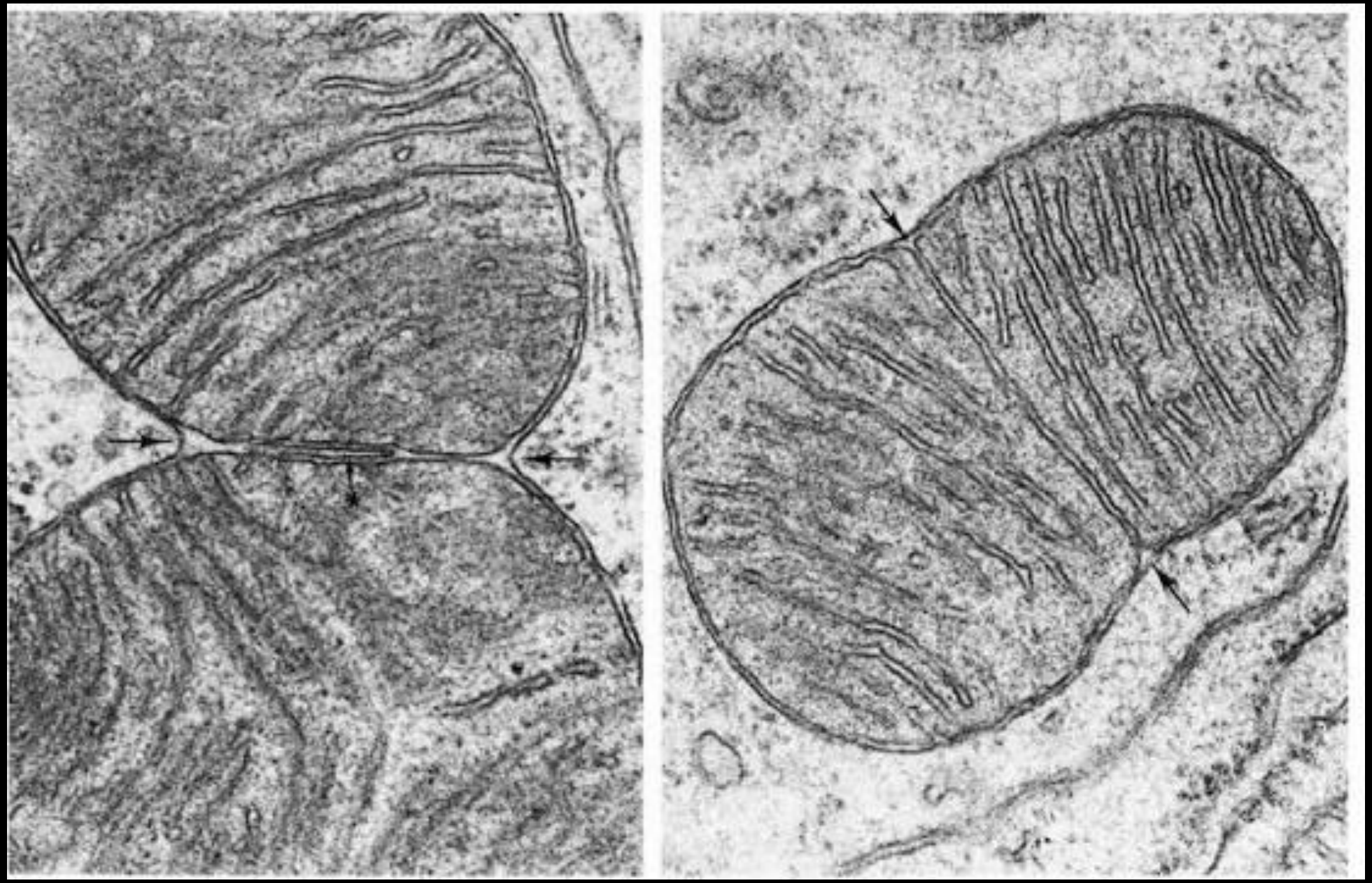



Red Label
BELL'S
Ballantine
FINEST
JIM BEAM
BOURBON
JACK DANIEL'S
No 7
Tennessee
WHISKEY
TULLAMORE
DEW
IRISH WHISKEY




Mitochondrion
Outer and inner membranes
Matrix
Cristae
0.1 µm


100 nm

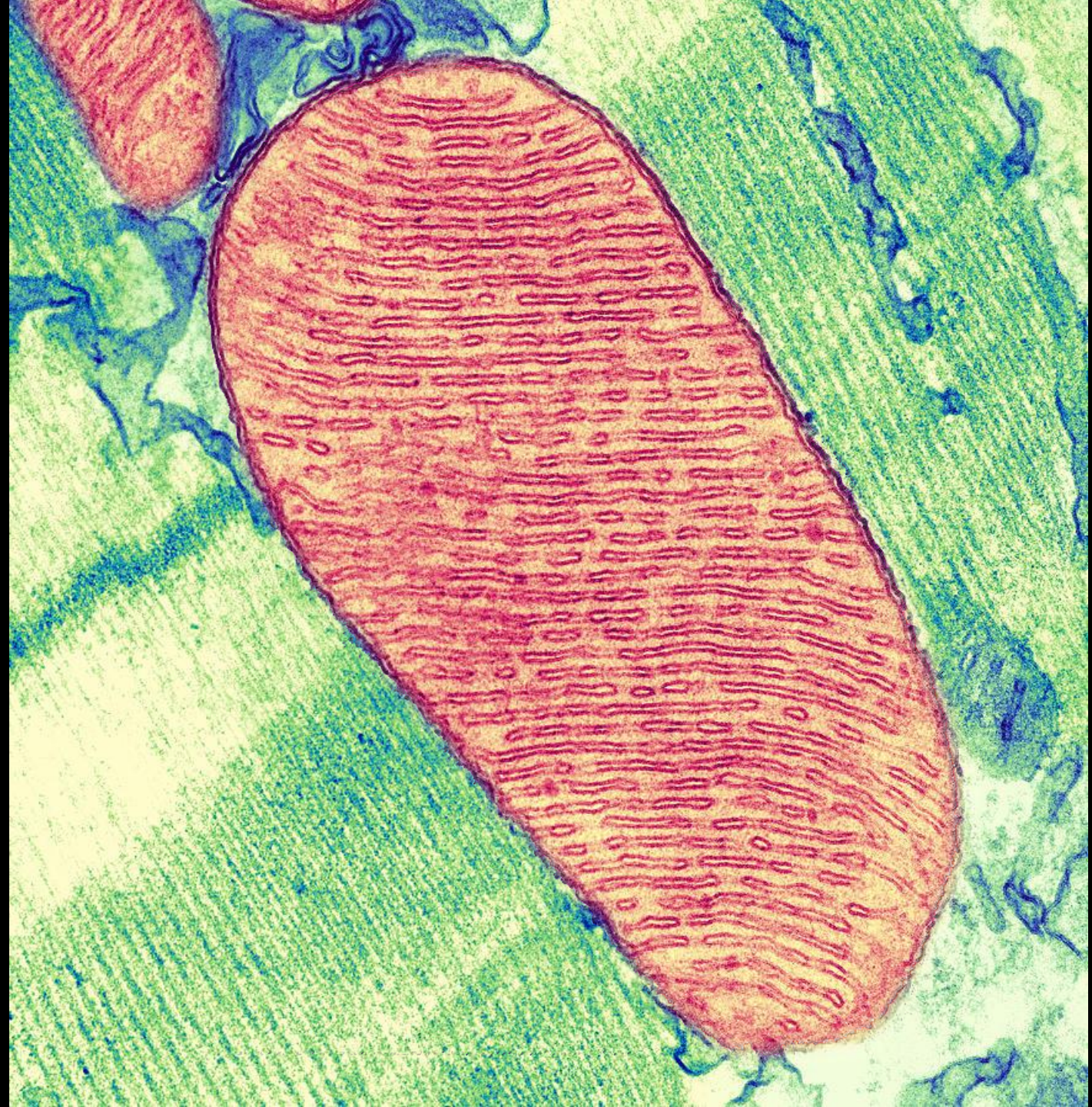


Transmission Electron Microscope



Ultramicrotomy





CELL ENERGY

Normal Cell

GLUCOSE (Carbs)



CELL ENERGY

Normal Cell

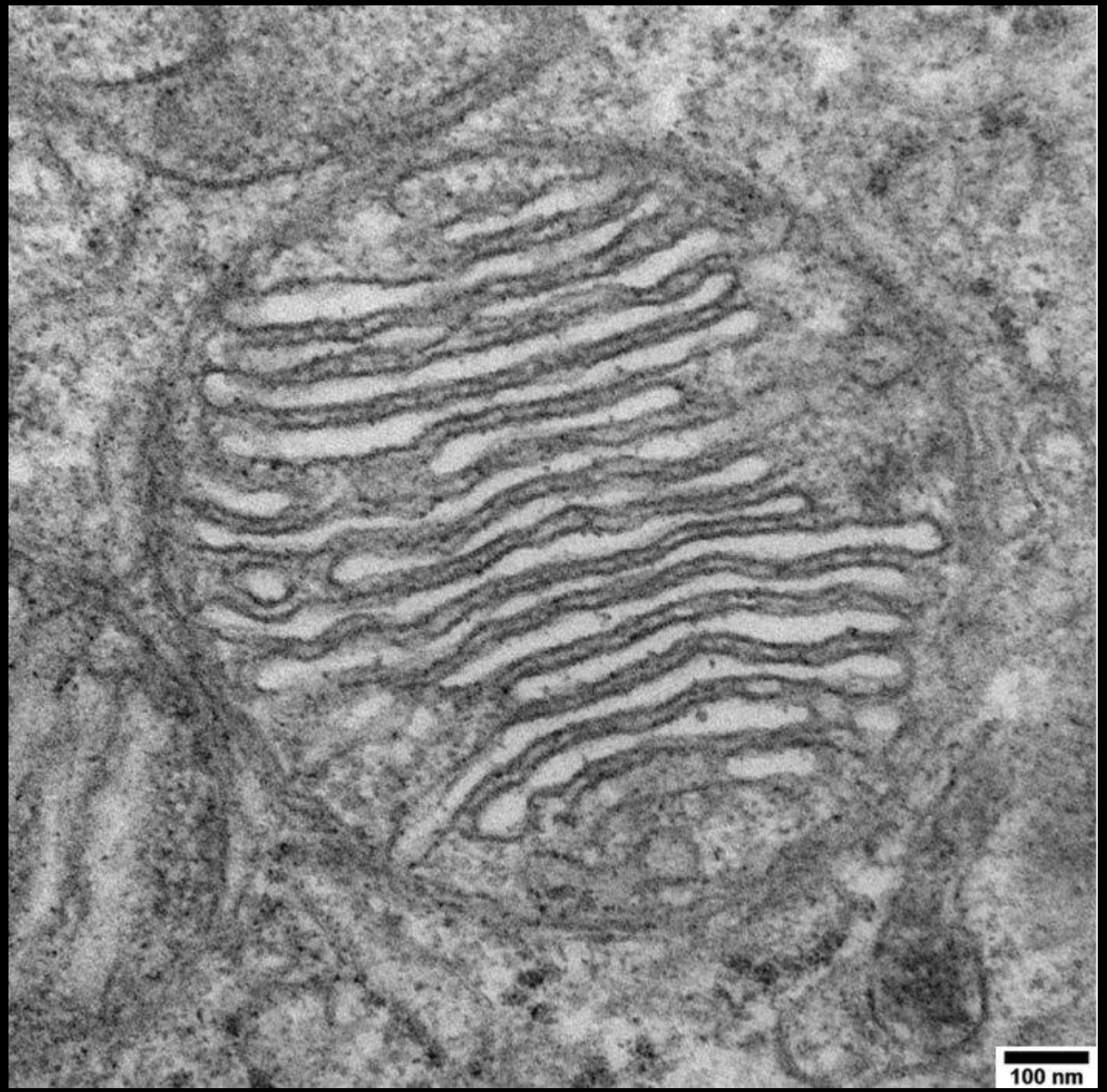
GLUCOSE (Carbs)	
FATS	

CELL ENERGY

	Normal Cell
GLUCOSE (Carbs)	
FATS	
PROTEIN	

CELL ENERGY

	Normal Cell
GLUCOSE (Carbs)	
FATS	
PROTEIN	
KETONES	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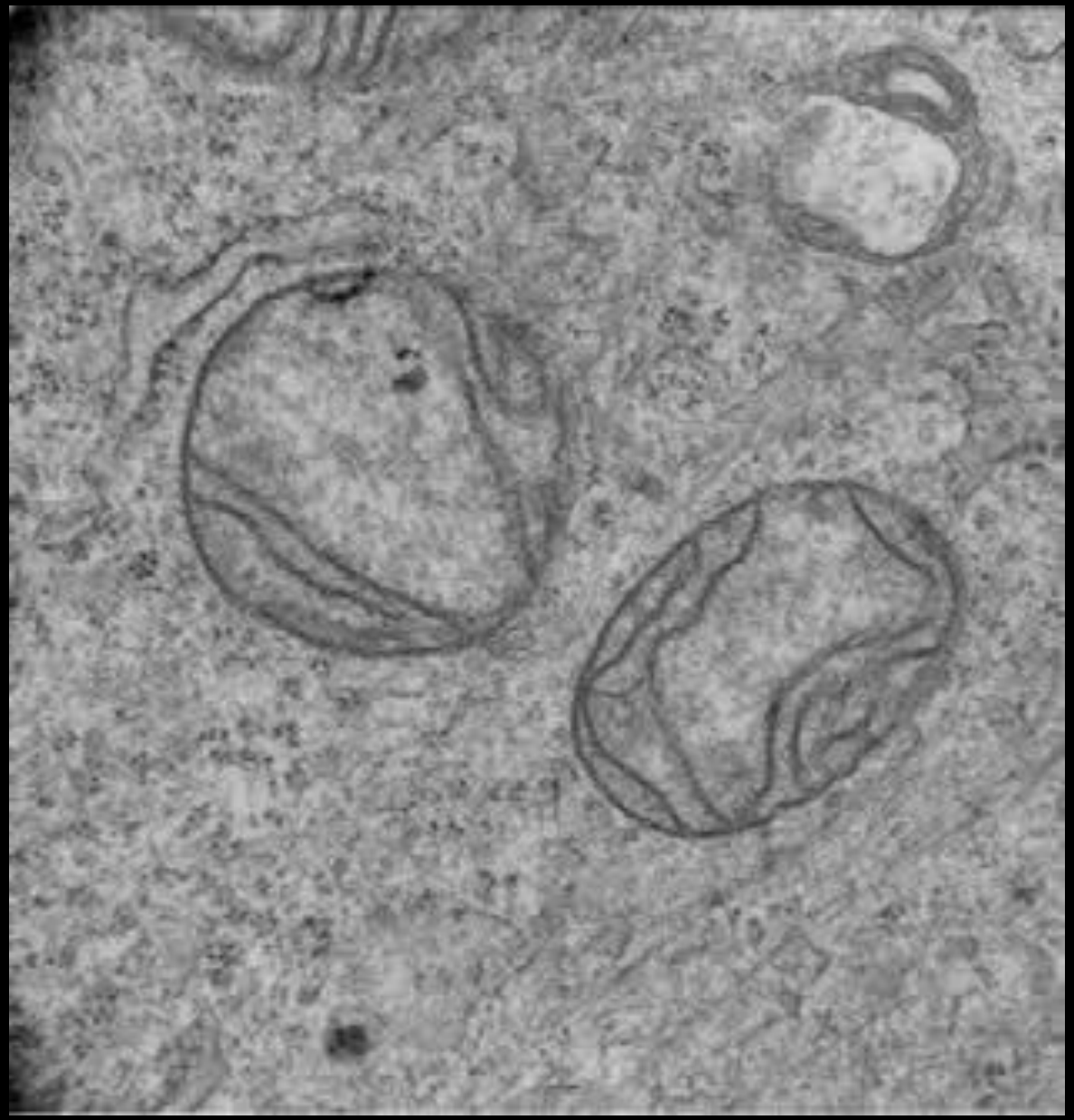
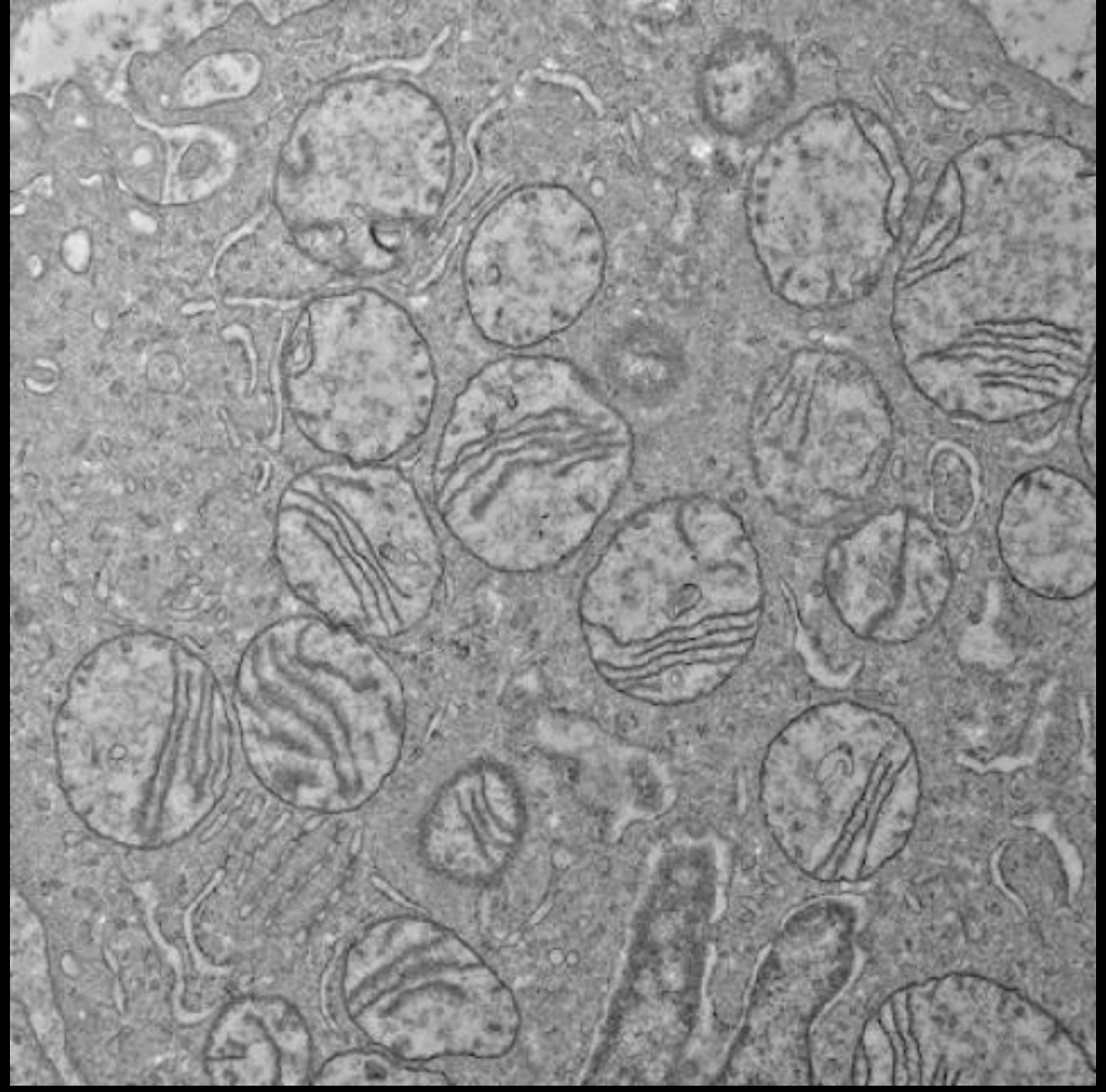
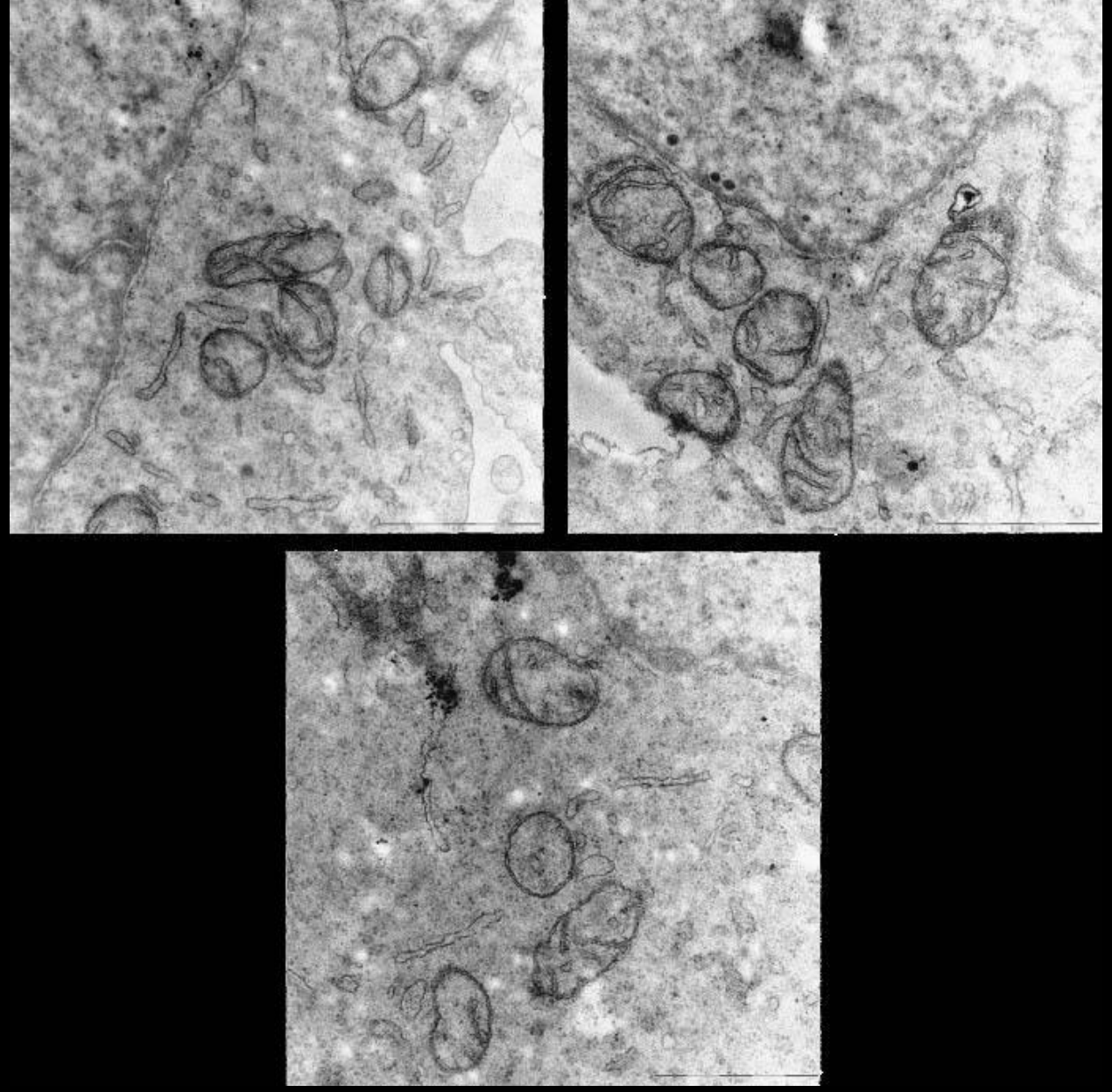


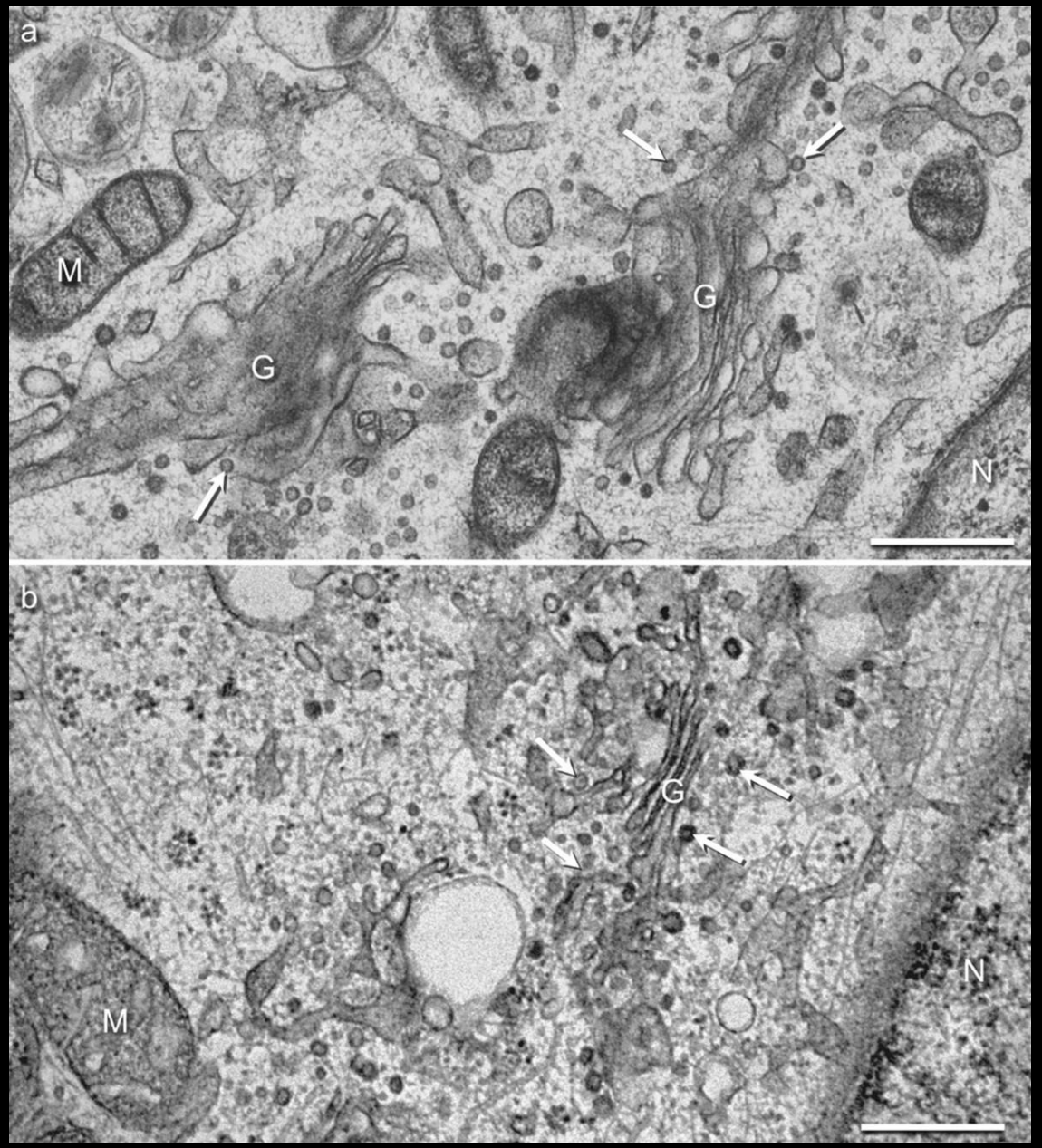
Pancreatic Cancer



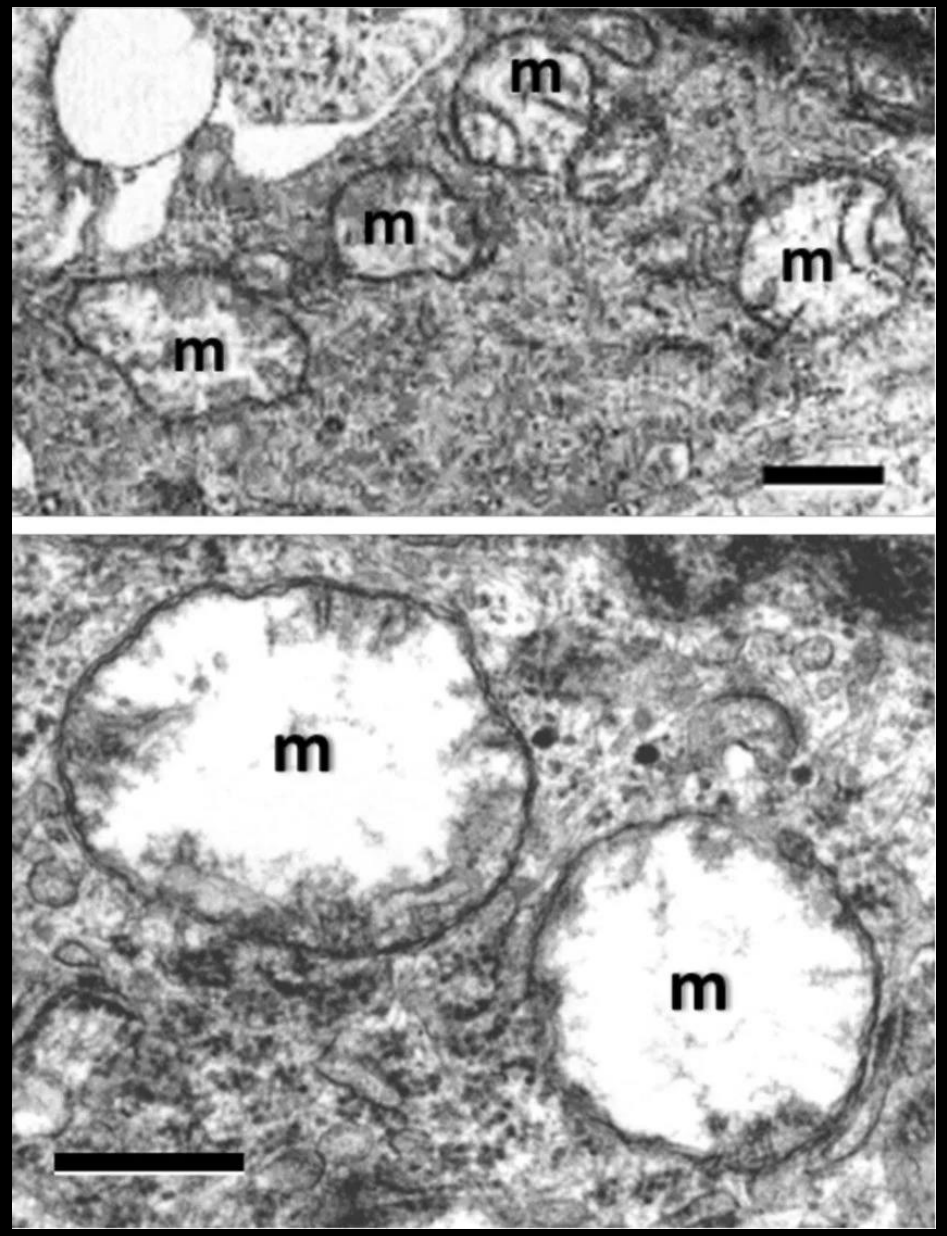
Kidney Cancer



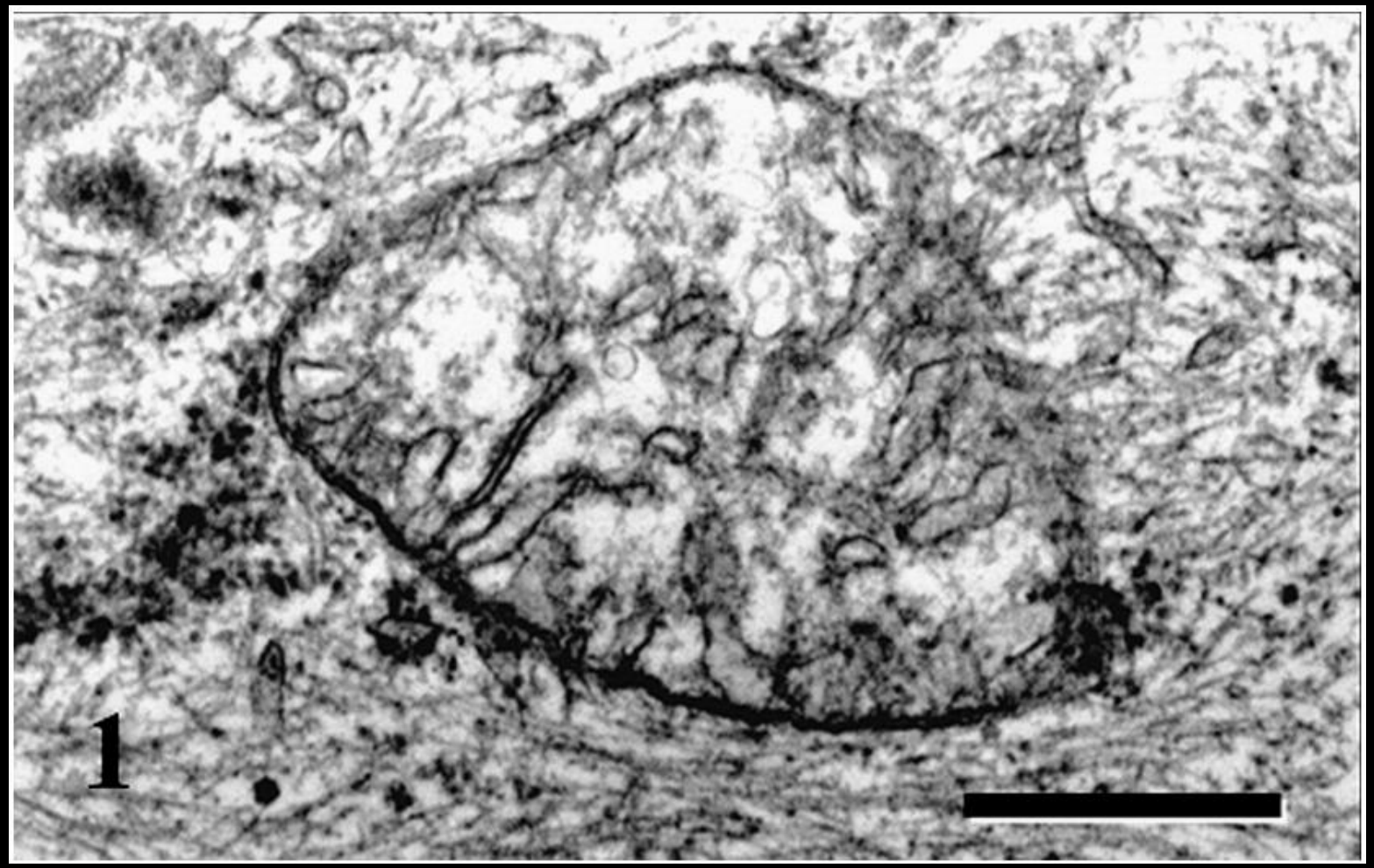
Acute Myeloid Leukaemia



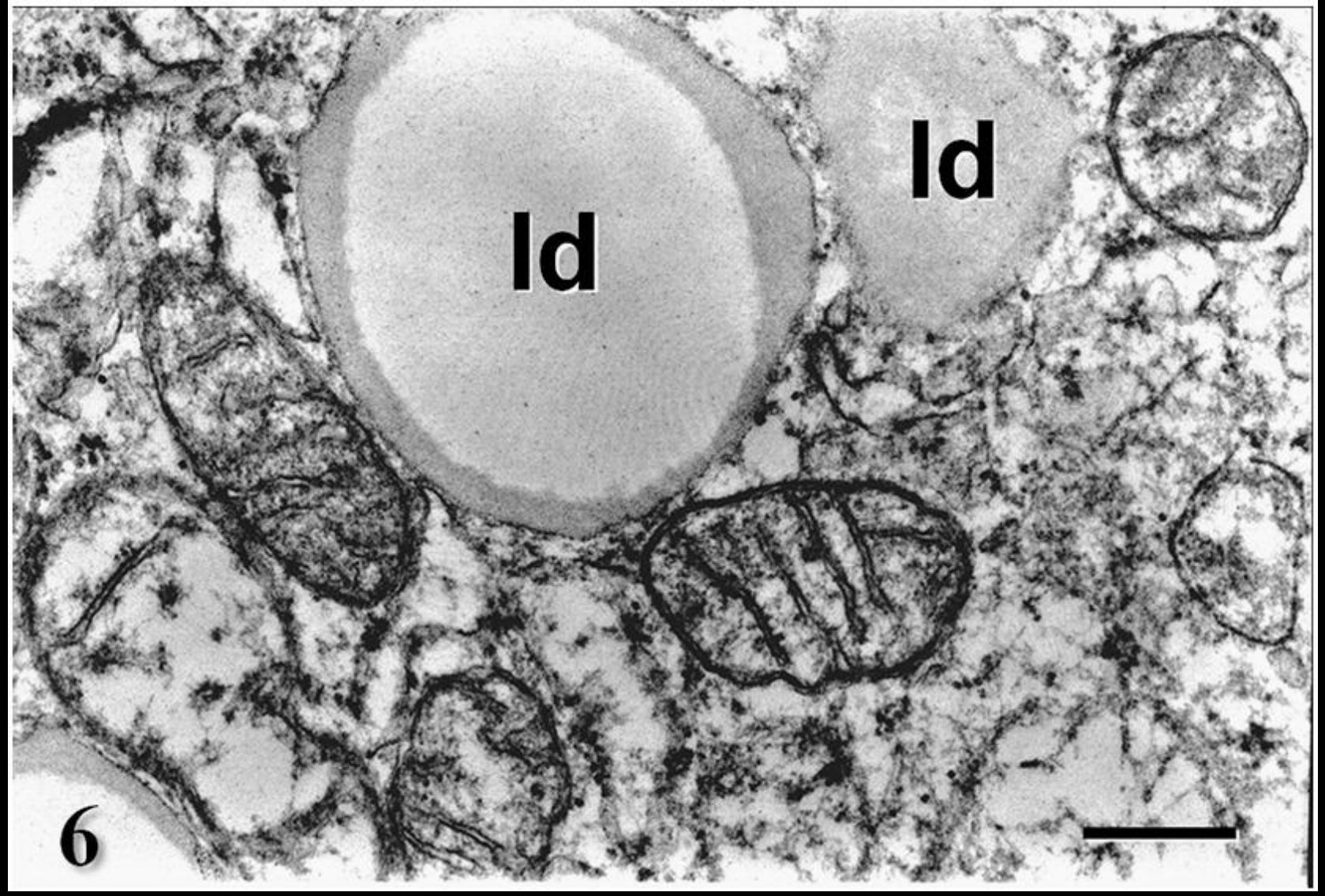
Glioblastoma



Glioblastoma



Glioblastoma



Cancer Cell Lipid Drops

CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	
FATS	✓	
PROTEIN	✓	
KETONES	✓	

CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	
PROTEIN	✓	
KETONES	✓	

WHAT A CANCER CELL NEEDS TO DO



X 100

WHAT HAPPENS AS A RESULT

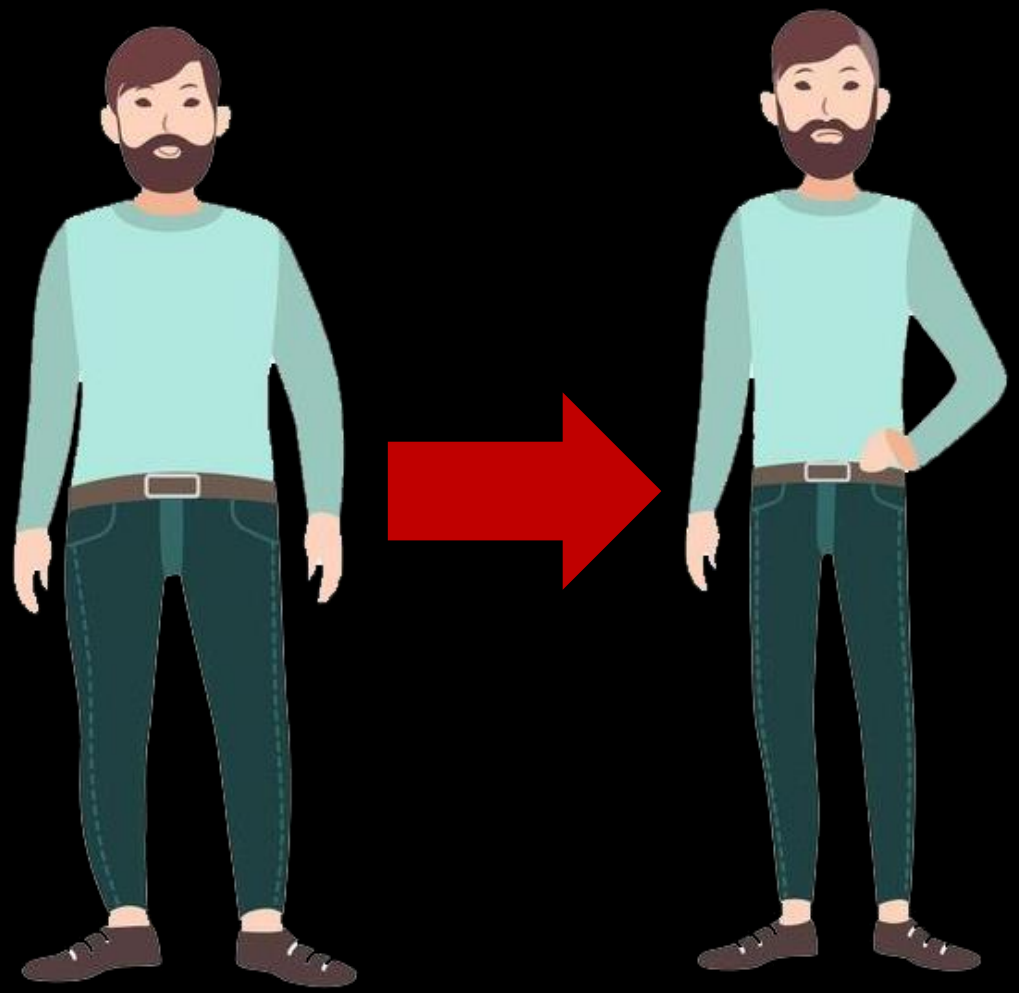


X 100



X 100

FROM WHERE DOES IT GET GLUCOSE?



+



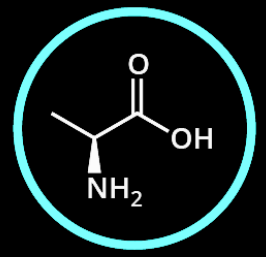
CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	
PROTEIN	✓	
KETONES	✓	

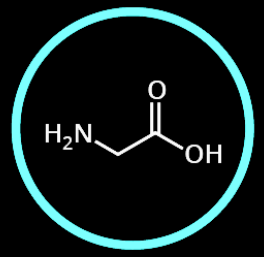
CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	
KETONES	✓	

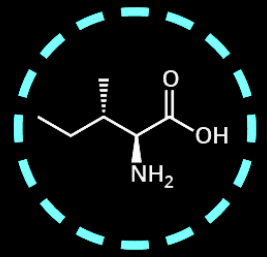

BROKEN SCIENCE
EVOLUTION OF THE REVOLUTION
ROKEN SCIENCE INTITIATIVE
EVOLUTION
OF THE
EVOLUTION
TOUR



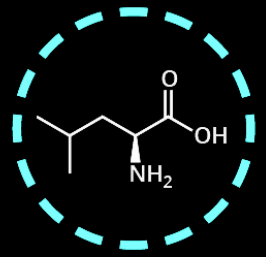
ALANINE A
ala



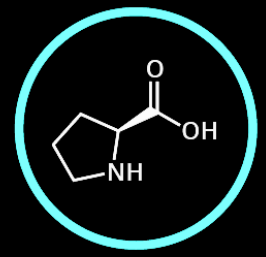
GLYCINE G
gly



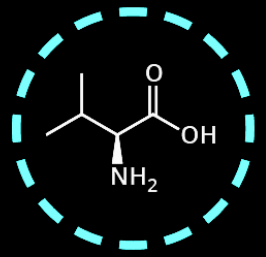
ISOLEUCINE I
ile



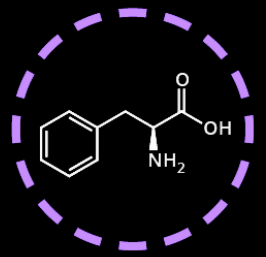
LEUCINE L
leu



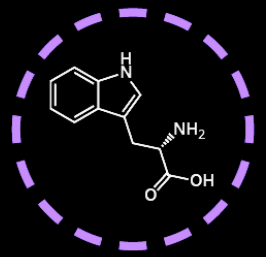
PROLINE P
pro



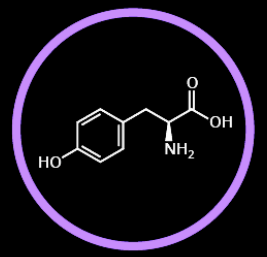
VALINE V
val



PHENYLALANINE F
phe



TRYPTOPHAN W
trp



TYROSINE Y
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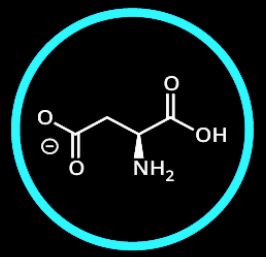
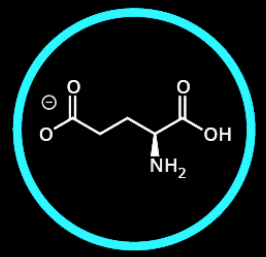


ASPARTIC ACID D
asp



GLUTAMIC ACID E
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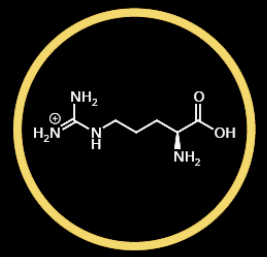

ARGININE R
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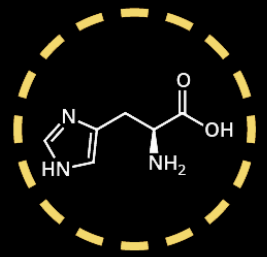
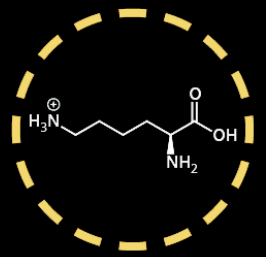


HISTIDINE H
his



LYSINE K
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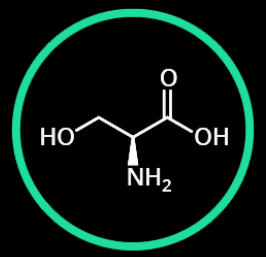
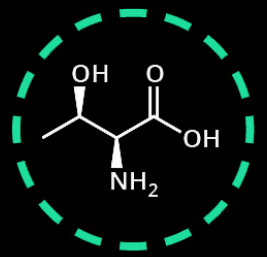
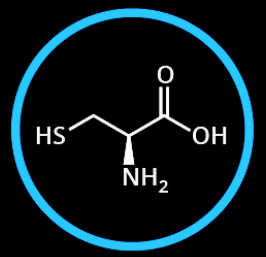


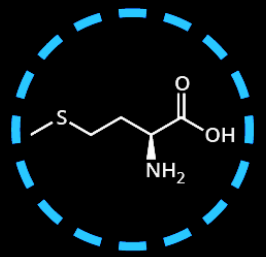
SERINE S
ser



THREONINE T
thr



CYSTEINE C
cys



METHIONINE M
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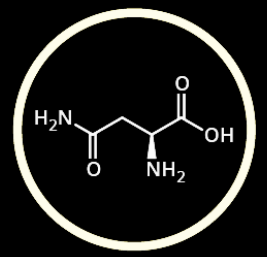
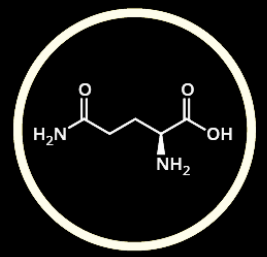
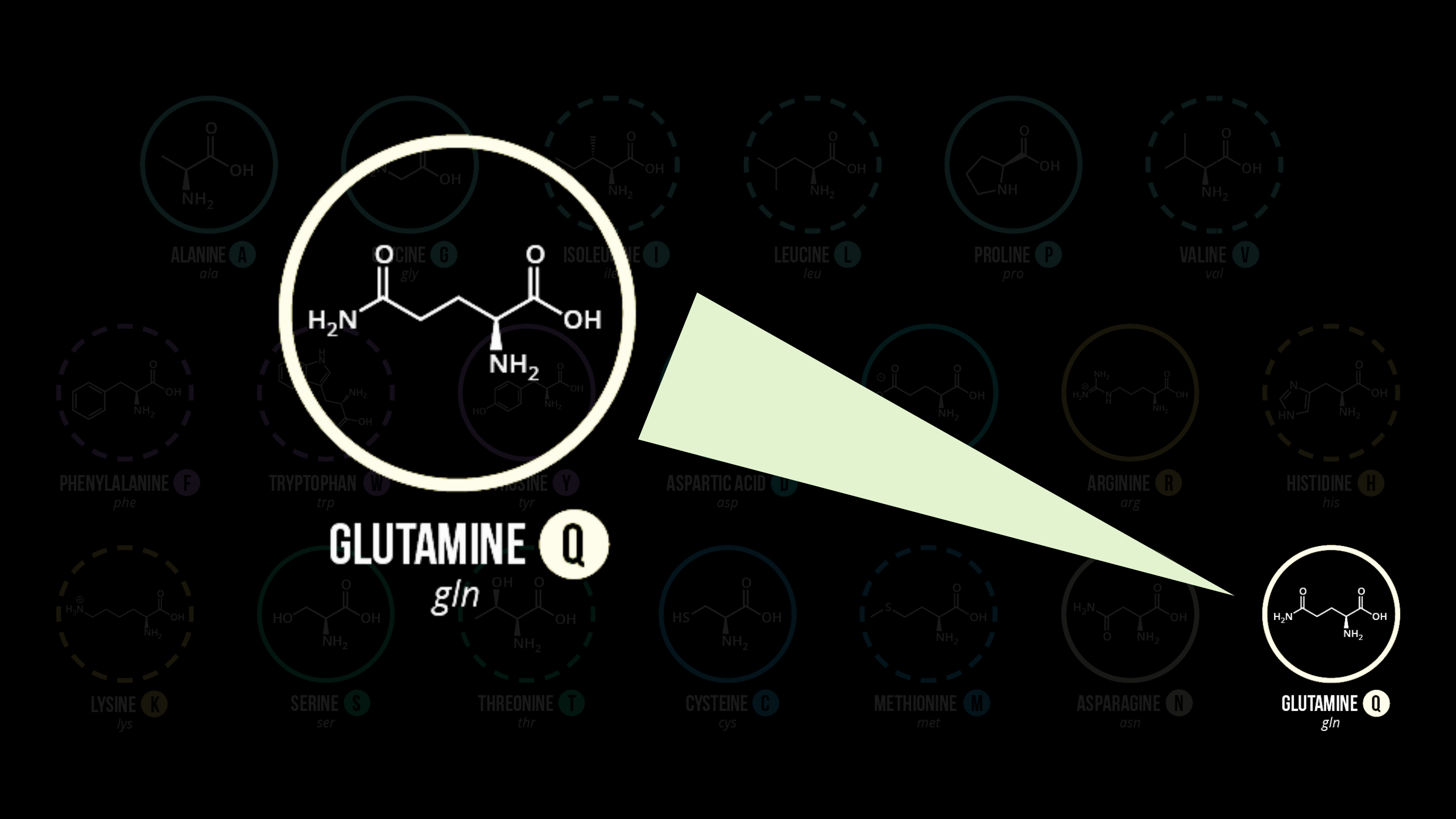


ASPARAGINE N
asn



GLUTAMINE Q
gln


ALANINE A
ala
LEUCINE L
leu
PROLINE P
pro
VALINE V
val
PHENYLALANINE F
phe
TRYPTOPHAN W
trp
ASPARTIC ACID D
asp
ARGININE R
arg
HISTIDINE H
his
GLUTAMINE Q
gln
LYSINE K
lys
SERINE S
ser
THREONINE T
thr
CYSTEINE C
cys
METHIONINE M
met
ASPARAGINE N
asn
GLUTAMINE Q
gln

CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	✓ GLUTAMINE
KETONES	✓	

WHAT A CANCER CELL NEEDS TO DO



X 100

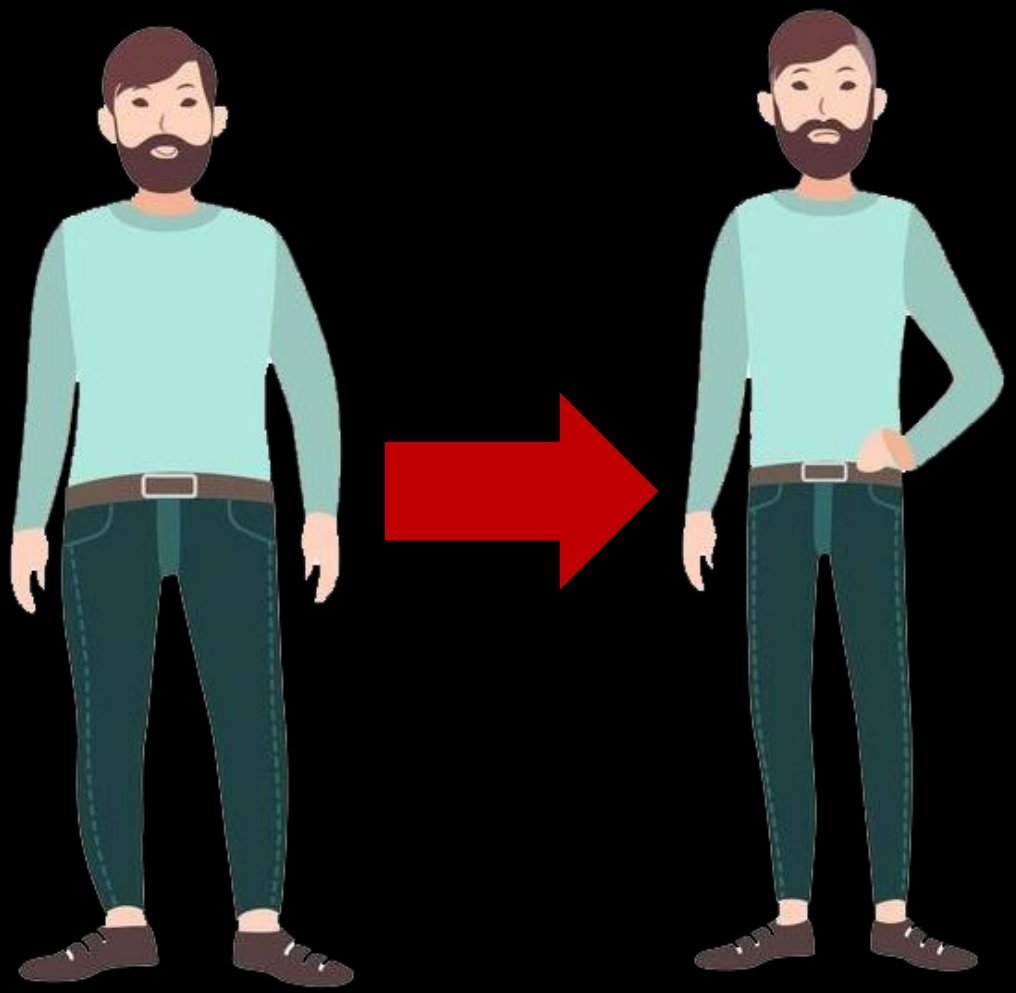
WHAT HAPPENS AS A RESULT



X 100

X 100

FROM WHERE DOES IT GET GLUTAMINE?



+



CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	GLUTAMINE ✓
KETONES	✓	

CELL ENERGY

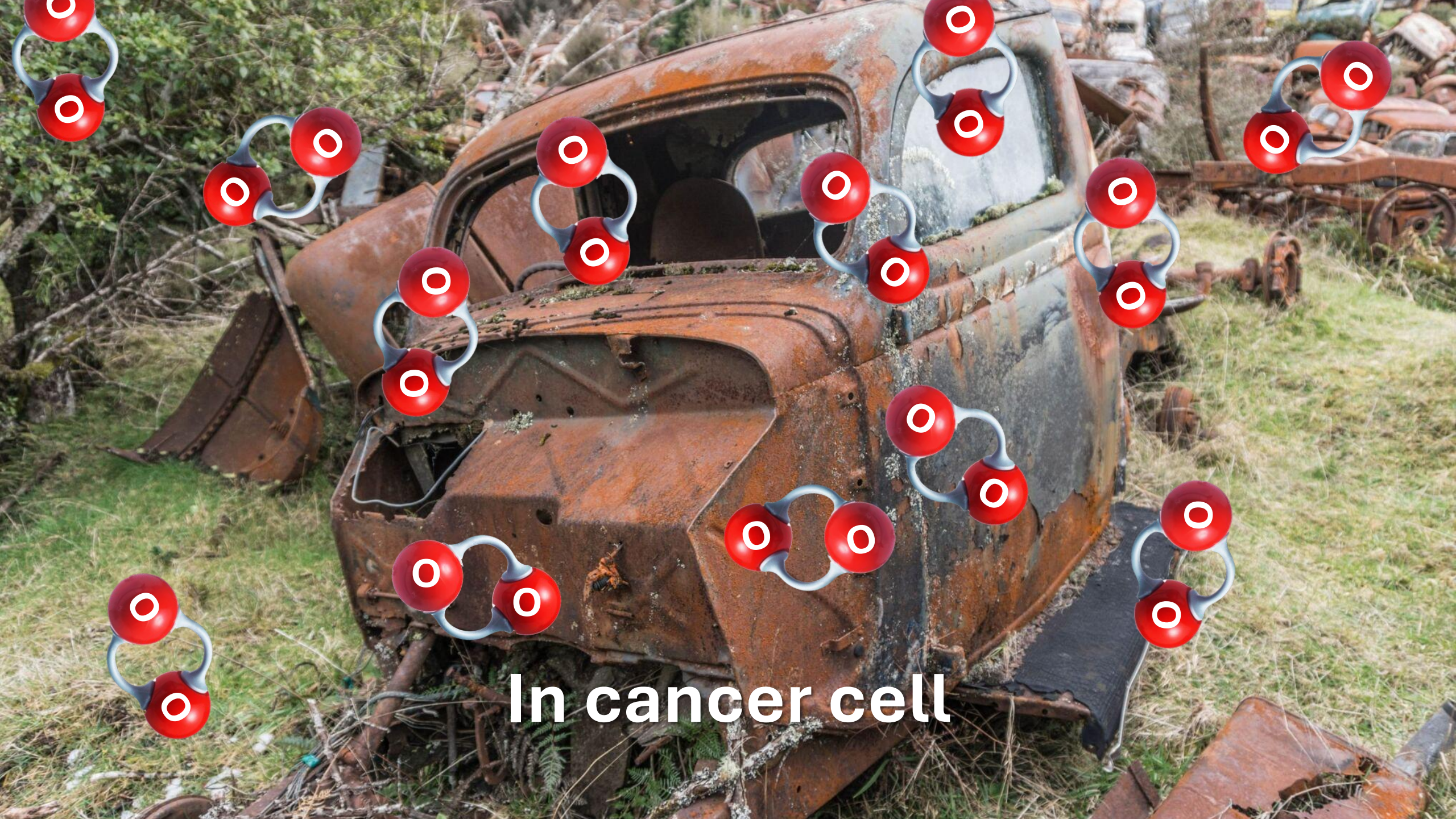
	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	GLUTAMINE ✓
KETONES	✓	✗

CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	GLUTAMINE ✓
KETONES	✓	✗
OXYGEN		

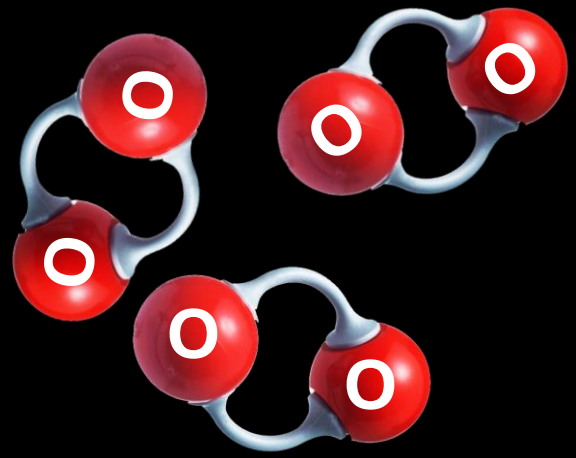
CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	GLUTAMINE ✓
KETONES	✓	✗
OXYGEN	✓	


In cancer cell

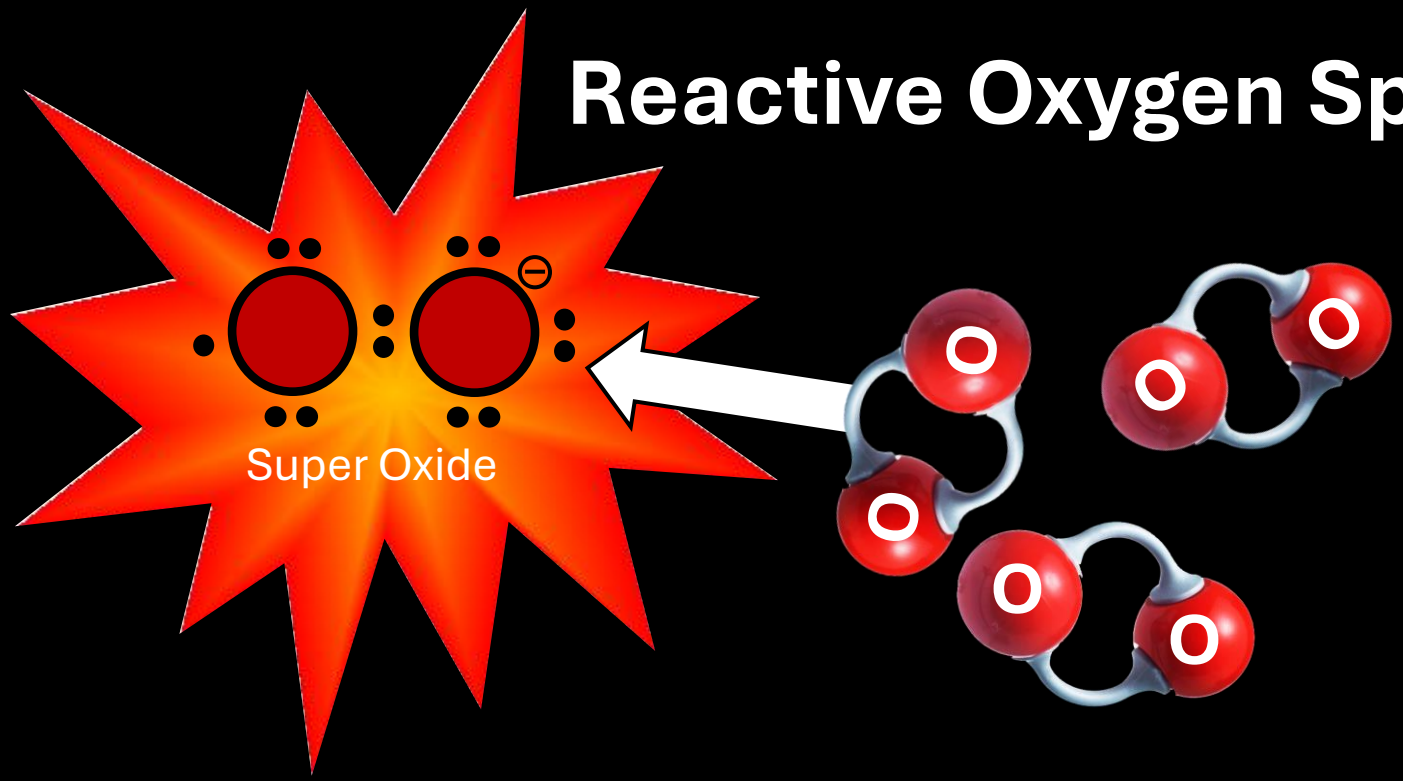

In cancer cell

Reactive Oxygen Species



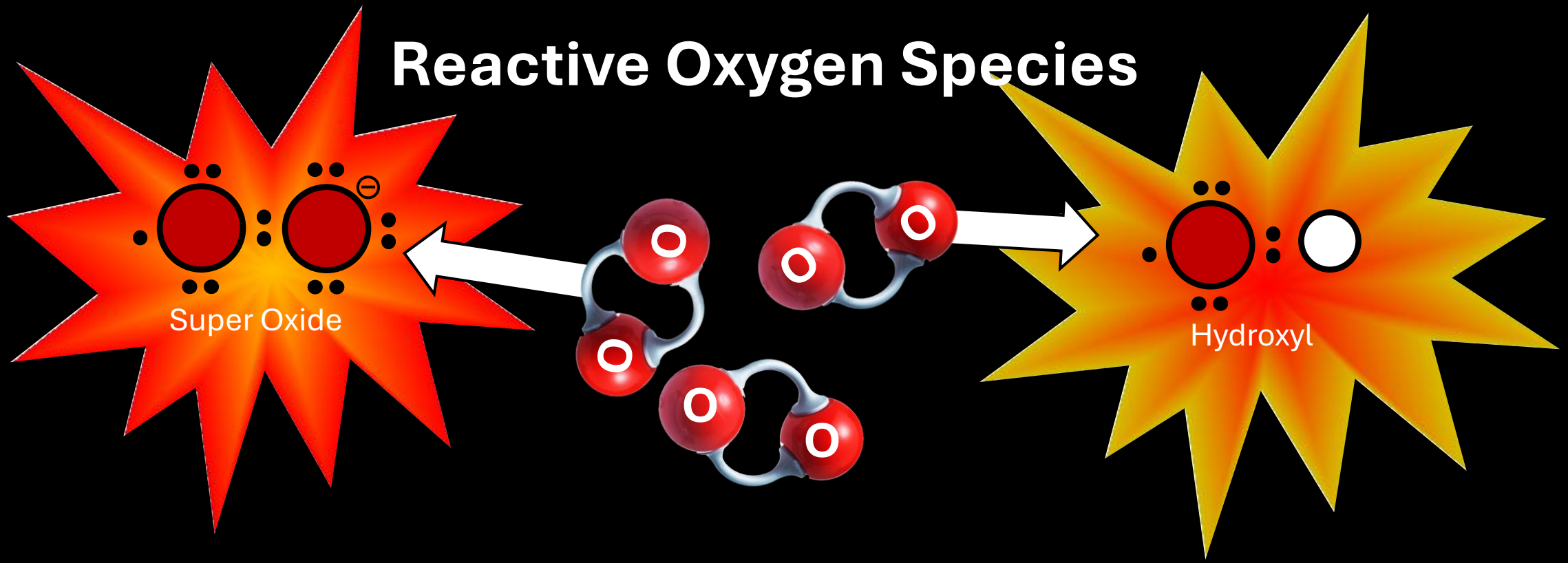
In cancer cell

Reactive Oxygen Species



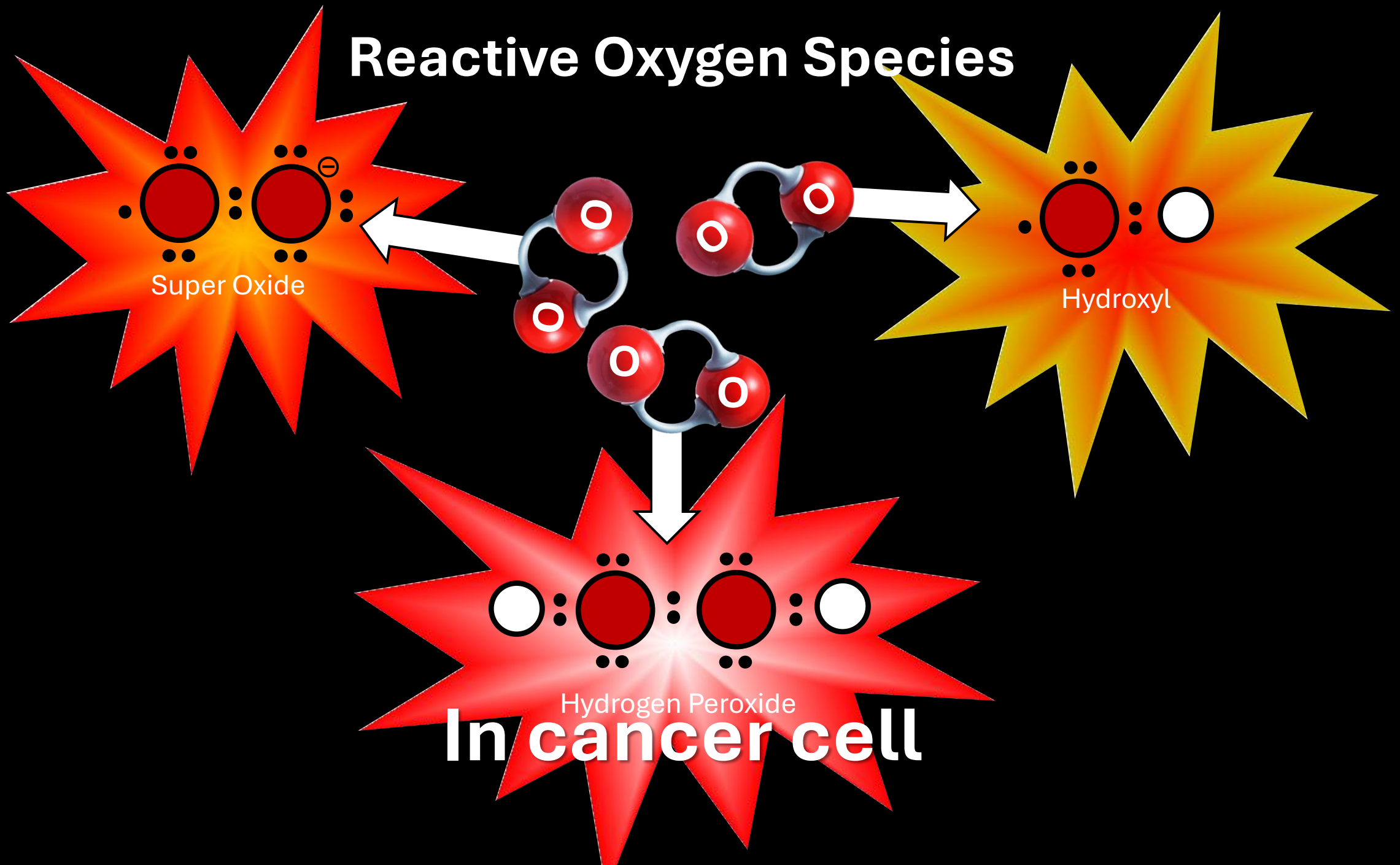
In cancer cell

Reactive Oxygen Species



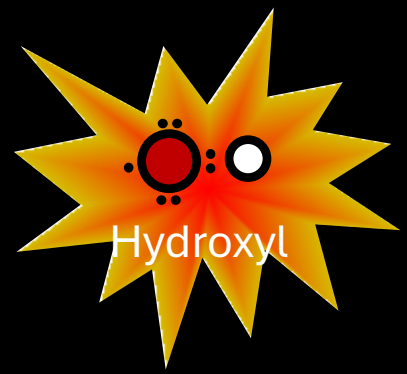
In cancer cell

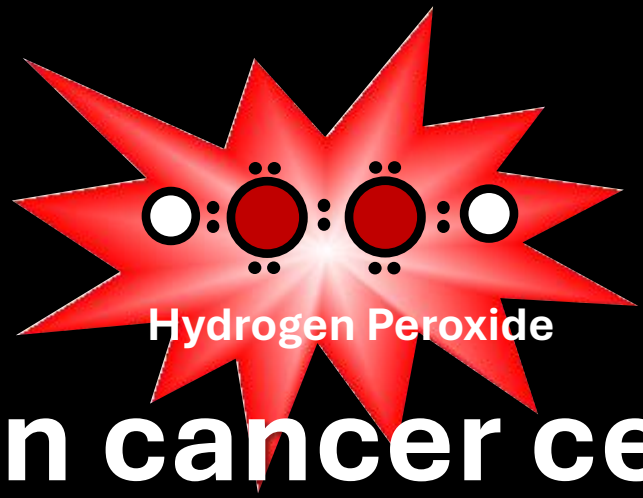
Reactive Oxygen Species



Reactive Oxygen Species

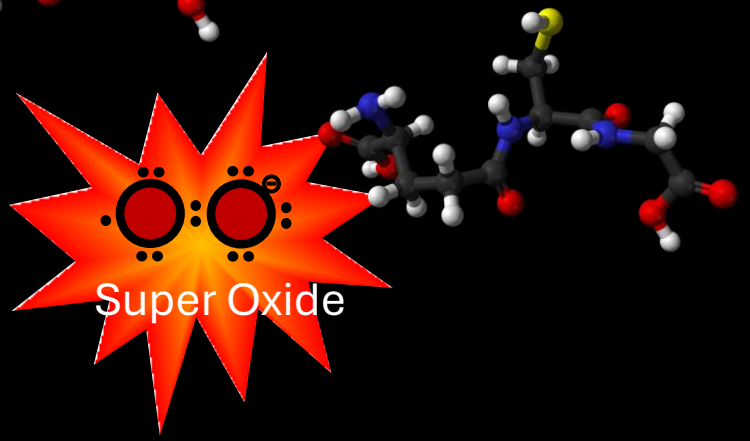


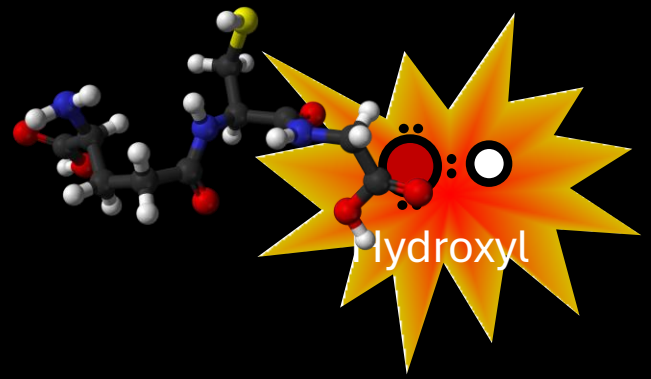


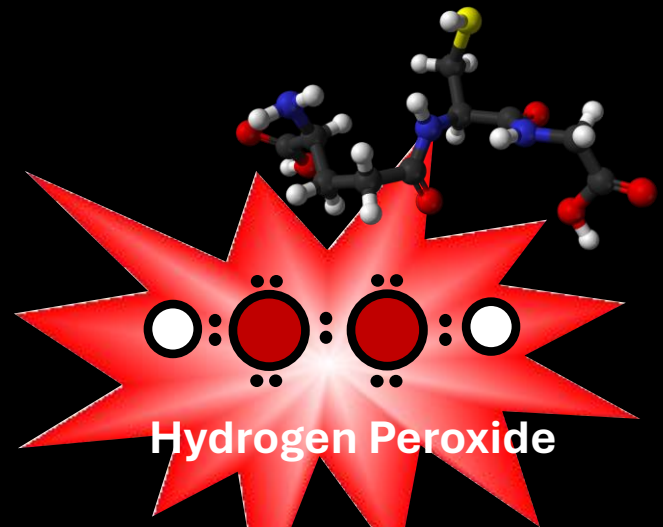


In cancer cell

Reactive Oxygen Species

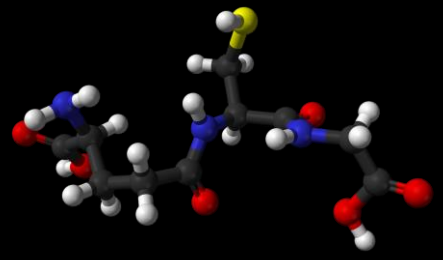


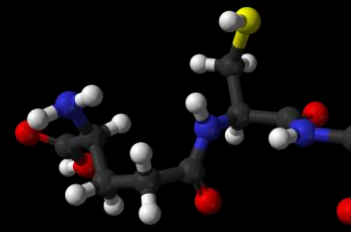


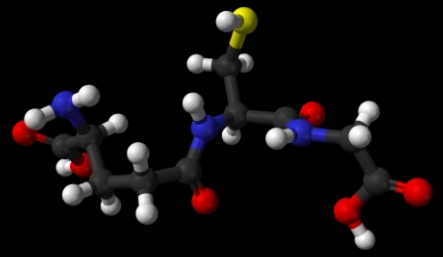


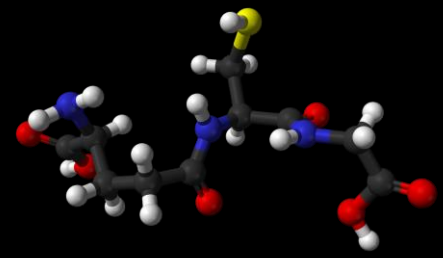
In cancer cell

Reactive Oxygen Species

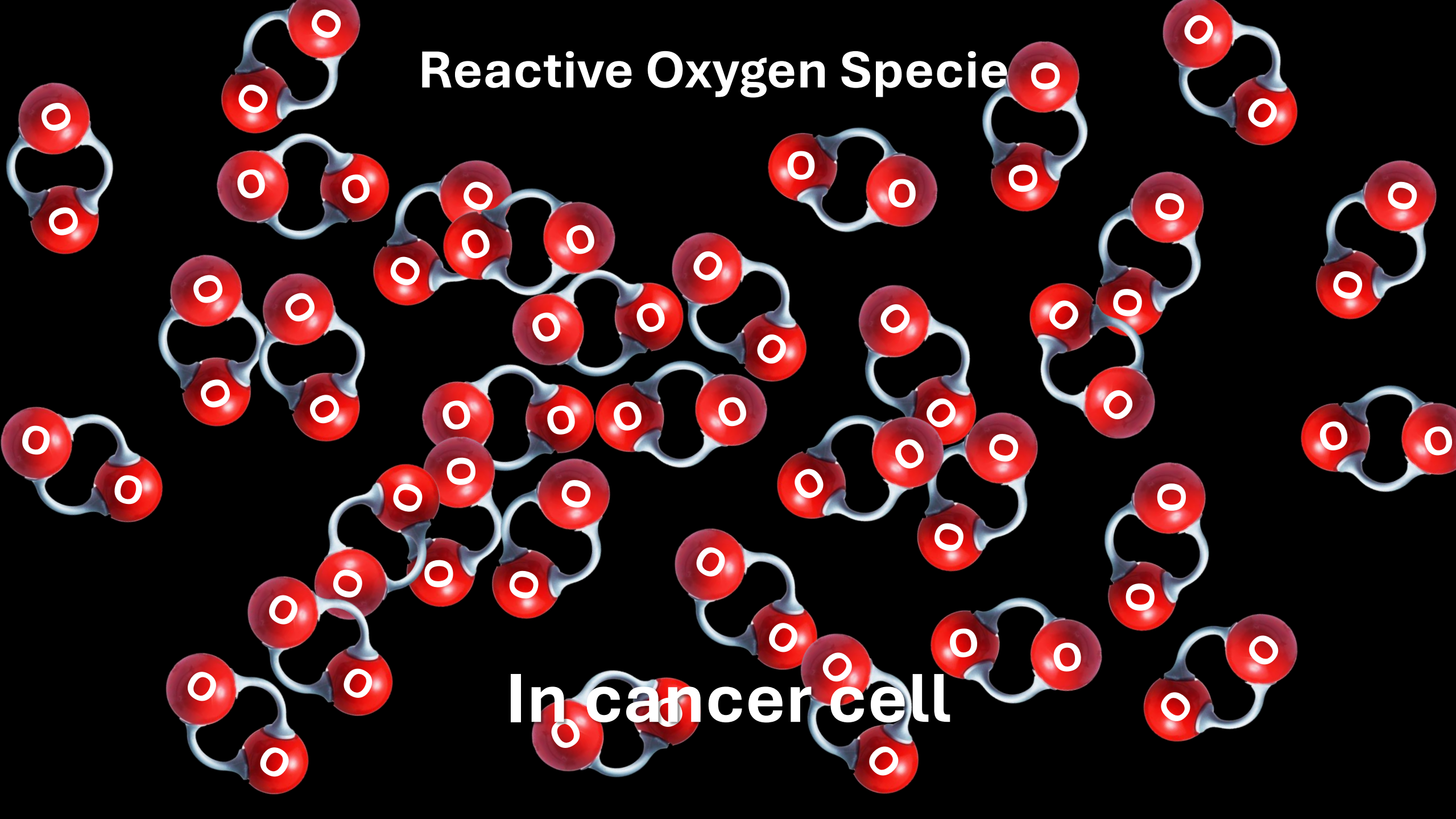


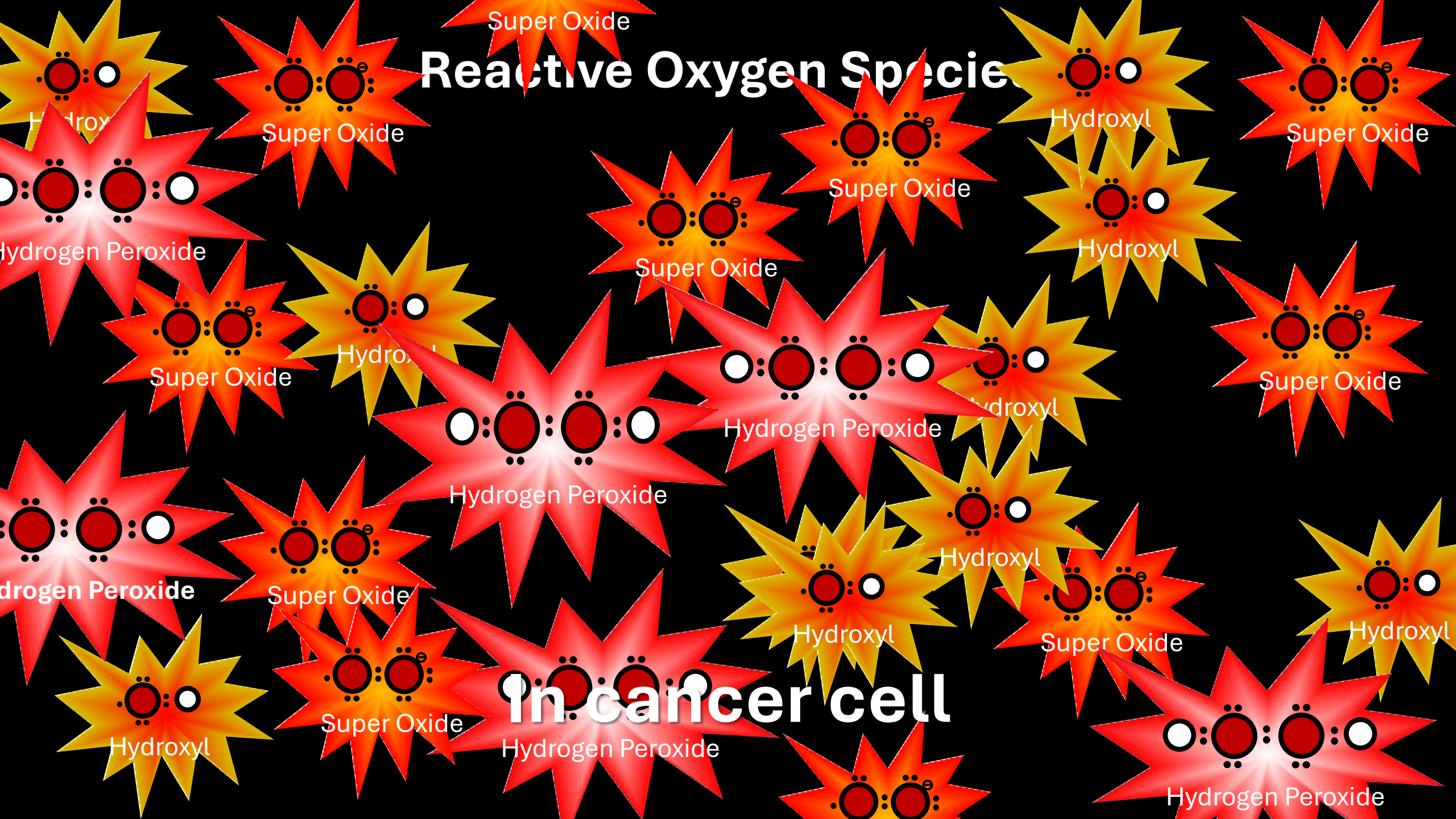






In cancer cell


Reactive Oxygen Specie
In cancer cell


Super Oxide
Reactive Oxygen Specie
Hydroxyl
Super Oxide
Super Oxide
Hydrogen Peroxide
Super Oxide
Super Oxide
Hydroxyl
Hydroxyl
Super Oxide
Super Oxide
Hydrogen Peroxide
Hydrogen Peroxide
Hydroxyl
Super Oxide
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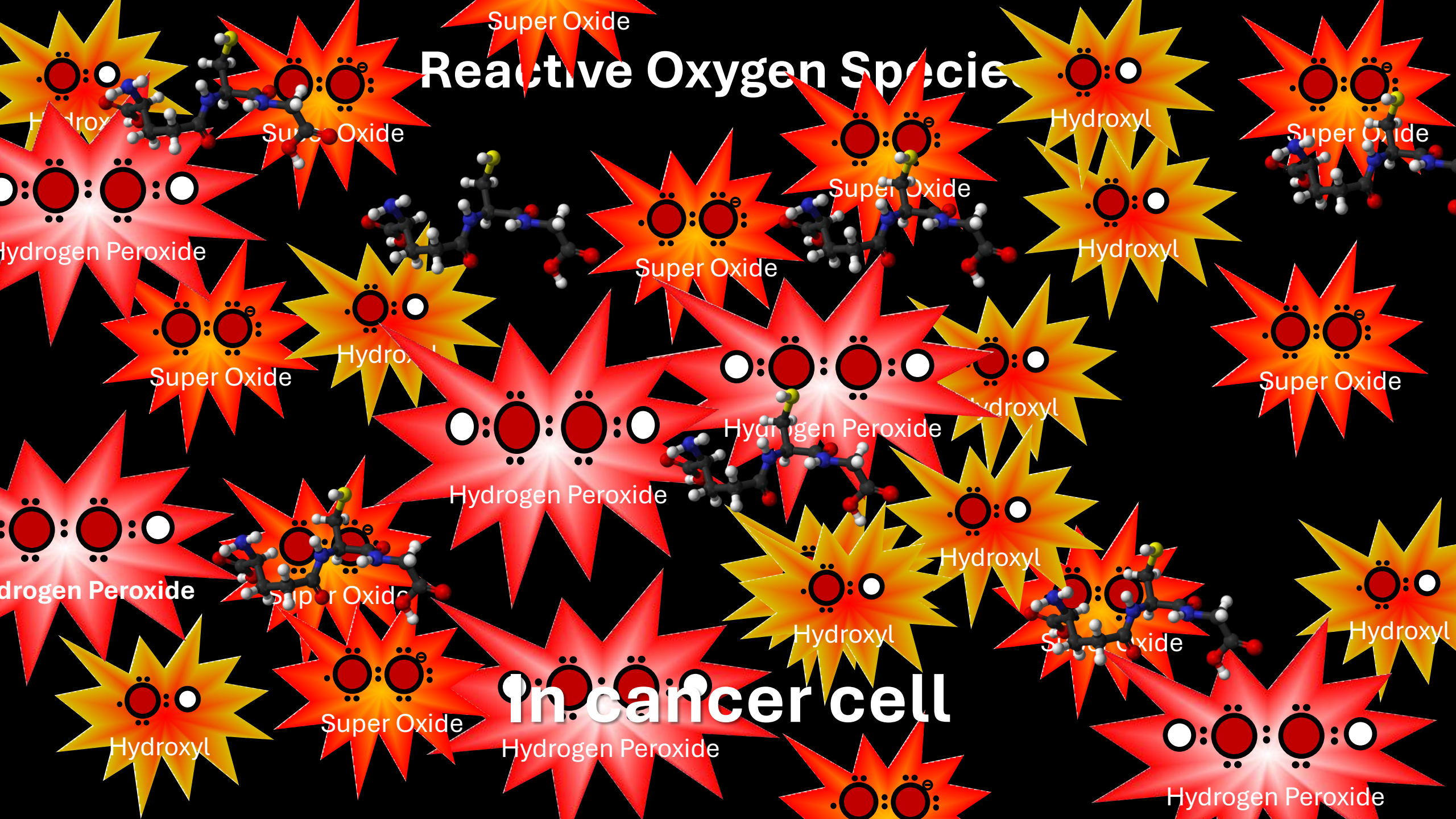
Super Oxide
Hydroxyl
Super Oxide
Hydroxyl
In cancer cell
Hydrogen Peroxide
Hydrogen Peroxide


Super Oxide
Reactive Oxygen Species
Hydroxyl
Super Oxide
Hydrogen Peroxide
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Super Oxide
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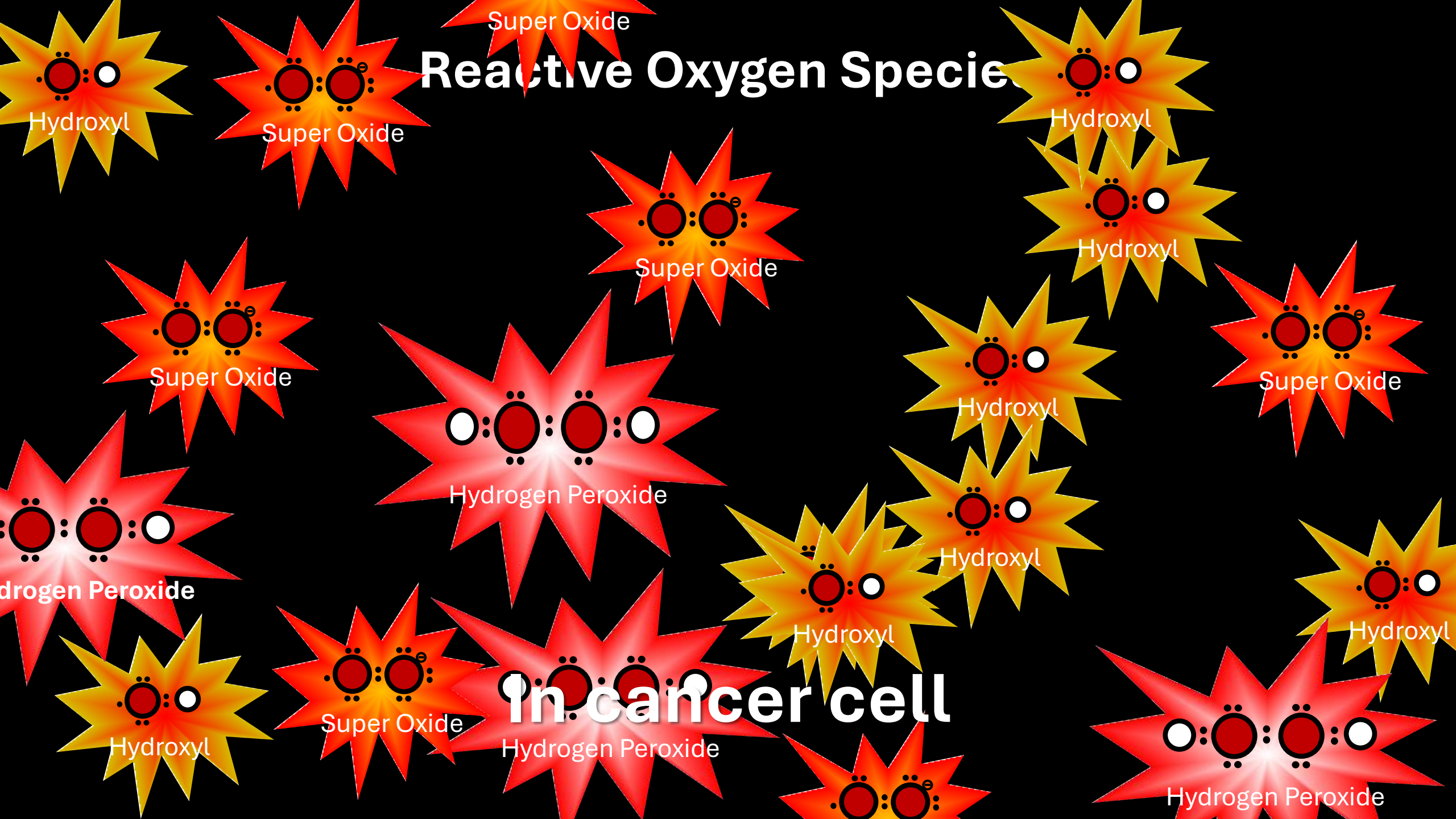
Super Oxide
In cancer cell
Hydrogen Peroxide
Hydroxyl
Hydrogen Peroxide


Super Oxide
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Hydroxyl
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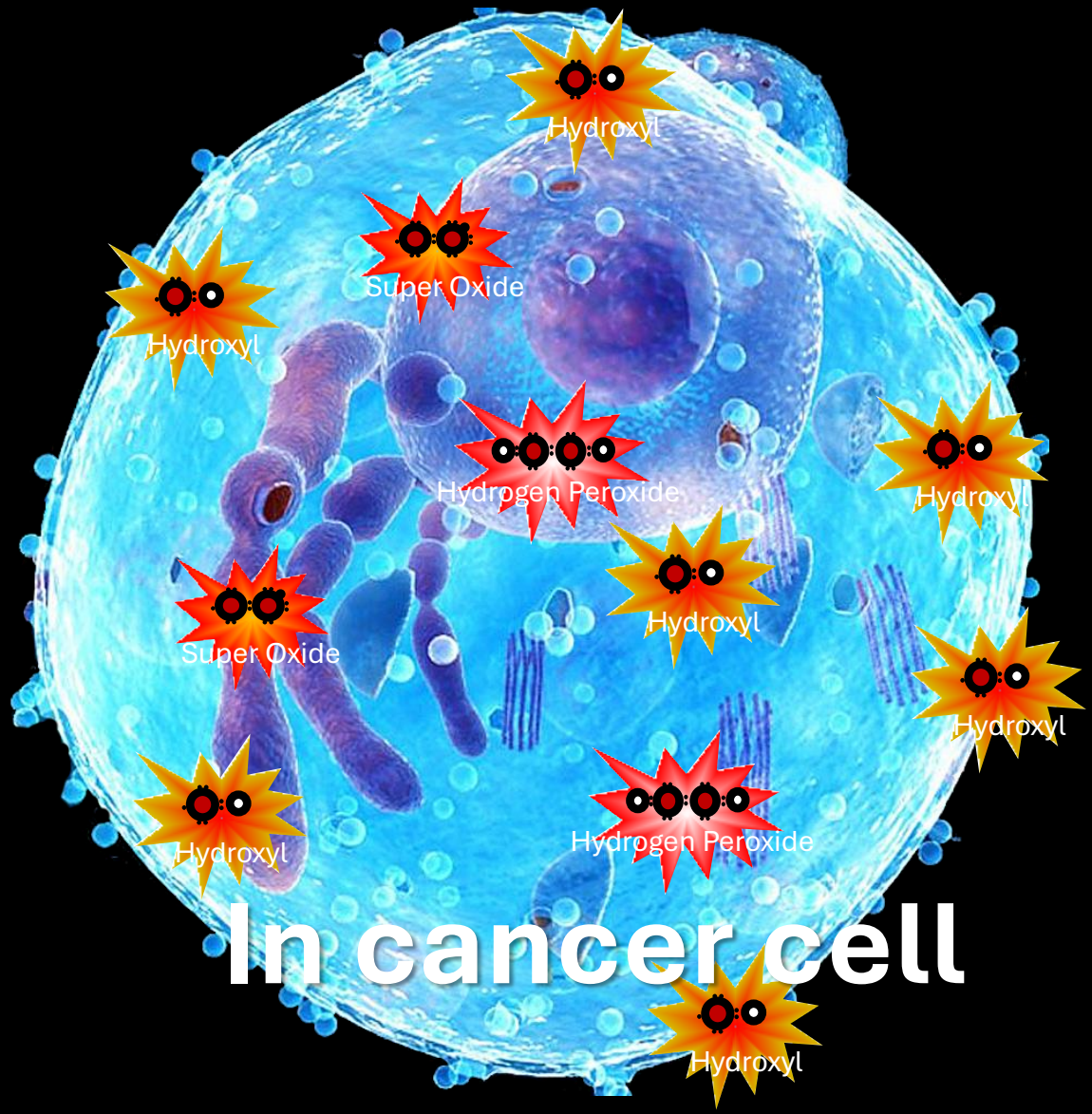
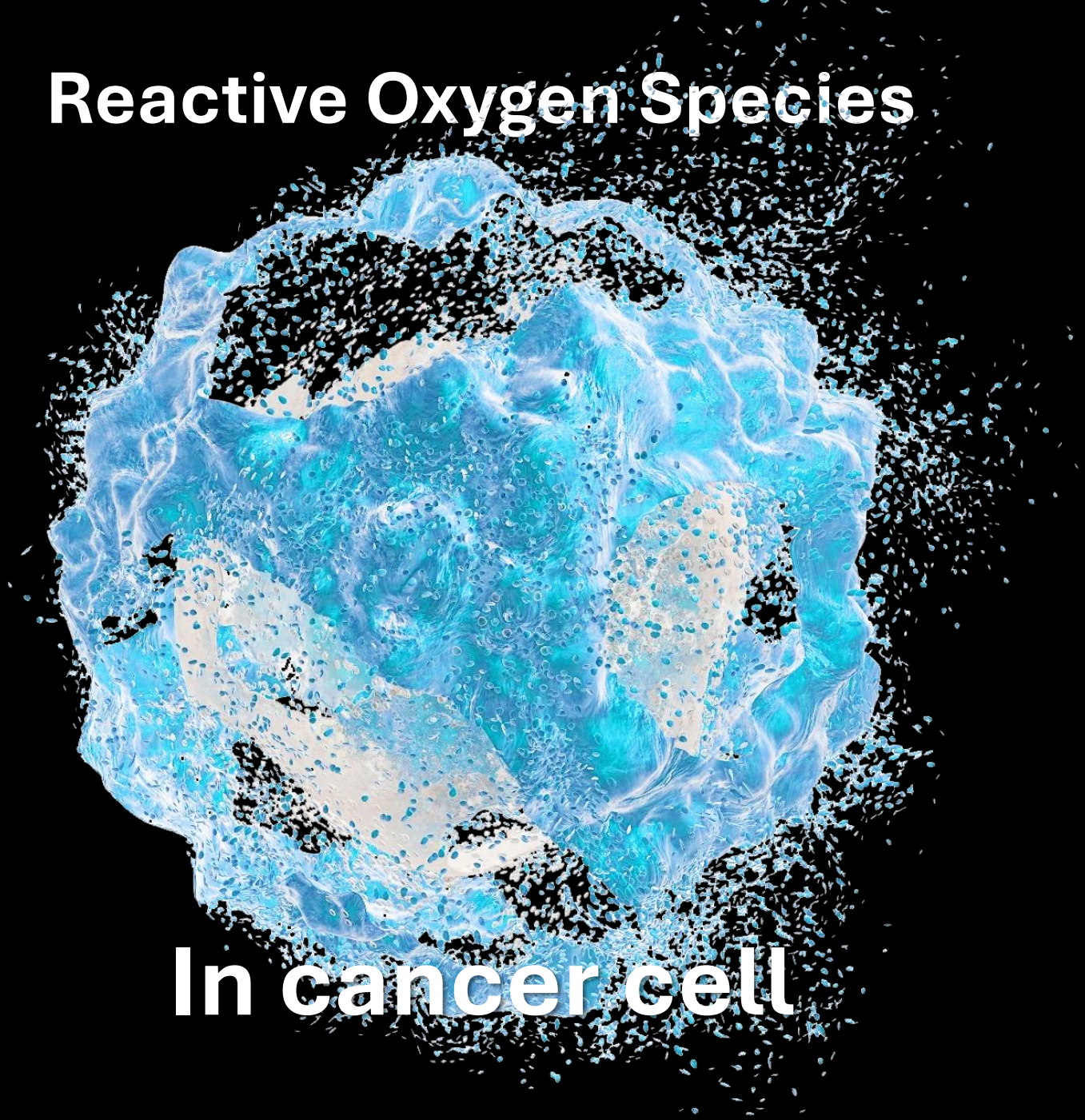
Hydroxyl
Super Oxide
In cancer cell
Hydrogen Peroxide
Hydrogen Peroxide

Reactive Oxygen Species



In cancer cell

Reactive Oxygen Species



In cancer cell

CELL ENERGY

	Normal Cell	Cancer Cell
GLUCOSE (Carbs)	✓	✓
FATS	✓	✗
PROTEIN	✓	GLUTAMINE ✓
KETONES	✓	✗
OXYGEN	✓	IN EXCESS ✗

Can we use all this to our advantage?

THE METABOLIC APPROACH

The metabolic approach is a non-toxic, lifelong cancer management framework that easily integrates with other treatments.









THE METABOLIC APPROACH

STAGE 1

PRESS


Calorie-Restricted Low-Glucose Diet

Route to Low-Glucose Diet

1. Enjoy all meats













Route to Low-Glucose Diet

1. Enjoy all meats
2. Enjoy all seafood









Route to Low-Glucose Diet

1. Enjoy all meats
2. Enjoy all seafood
3. Enjoy all oils & fats







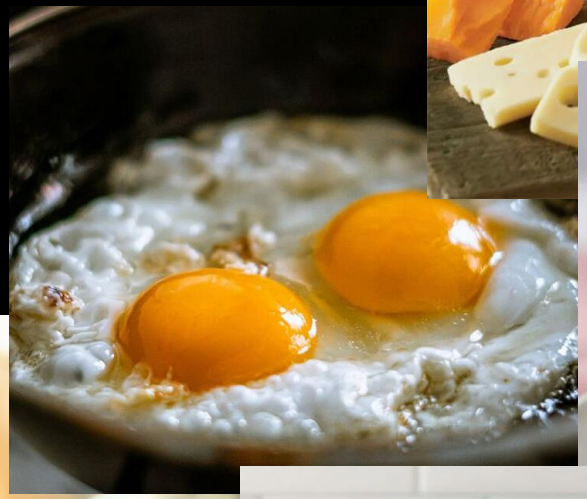






Route to Low-Glucose Diet

1. Enjoy all meats
2. Enjoy all seafood
3. Enjoy all oils & fats
4. Enjoy most diary





Route to Low-Glucose Diet

1. Enjoy all meats
2. Enjoy all seafood
3. Enjoy all oils & fats
4. Enjoy most diary
5. Enjoy all green veg.











Route to Low-Glucose Diet

1. Remove sugar







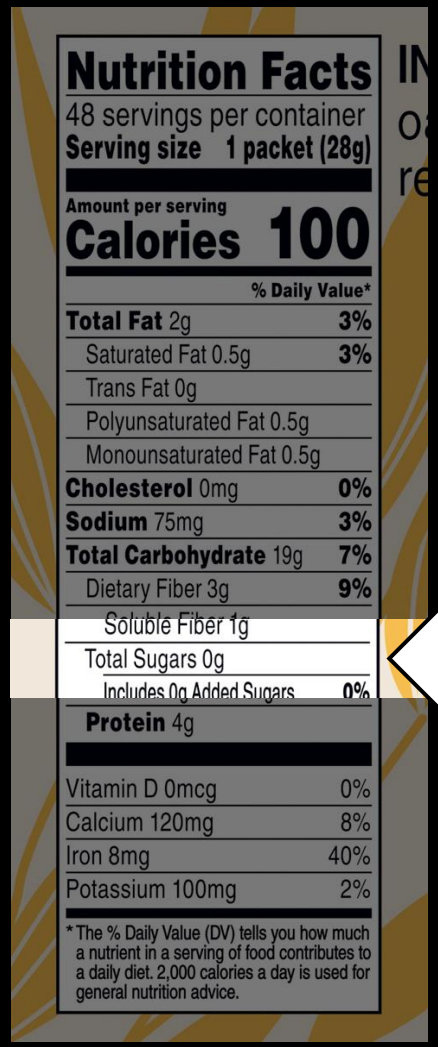








Route to Low-Glucose Diet

















Route to Low-Glucose Diet

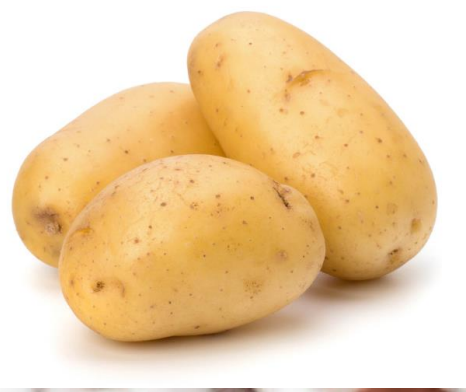
1. Remove sugar
2. Remove grains



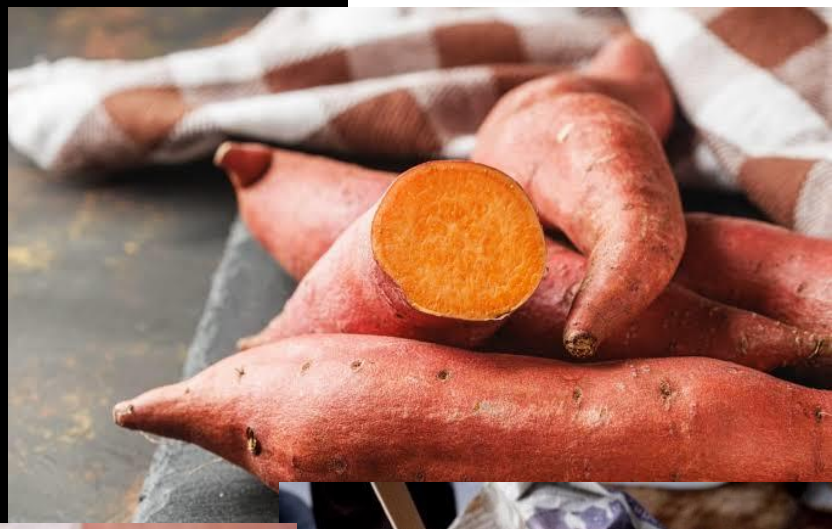





Route to Low-Glucose Diet



1. Remove sugar
2. Remove grains
3. Remove HS tubers







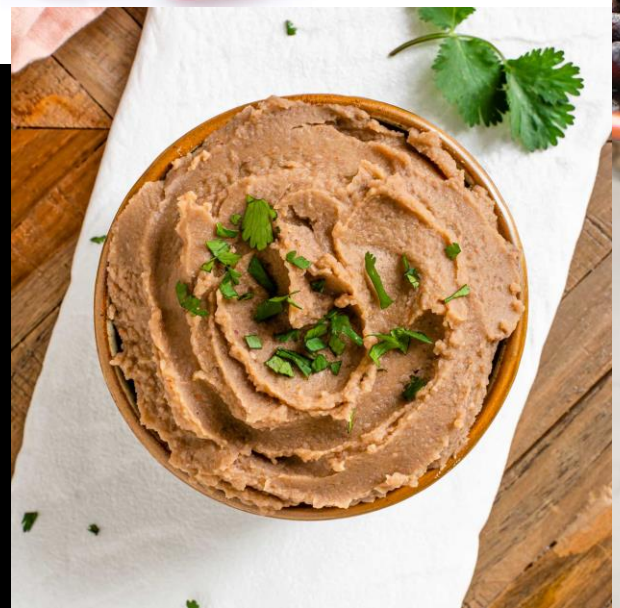
Route to Low-Glucose Diet

1. Remove sugar
2. Remove grains
3. Remove HS tubers
4. Remove HS legumes











Route to Low-Glucose Diet

Nutrition Facts

128 SERVINGS PER CONTAINER
Serving size 1 TBSP (15ML)

	Per Serving
Calories	**55**
	% Daily Value*
Total Fat 5g	6%
Sat. Fat 3g	15%
Trans Fat 0g	
Cholest. 20g	7%
Sodium 5mg	0%
Total Carb. 0g	0%
Dietary Fiber 0g	0%
Total Sugars 0g	
Incl. Added Sugars 0g	
Protein 1g	
Vitamin D 2mcg	10%
Calcium 10mg	1%
Iron 0mg	0%
Potassium 11mg	0%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition.









Supplementation

Multivitamin Tablets

Omega 3 oils

Vitamin D3

Calcium

B Vitamins

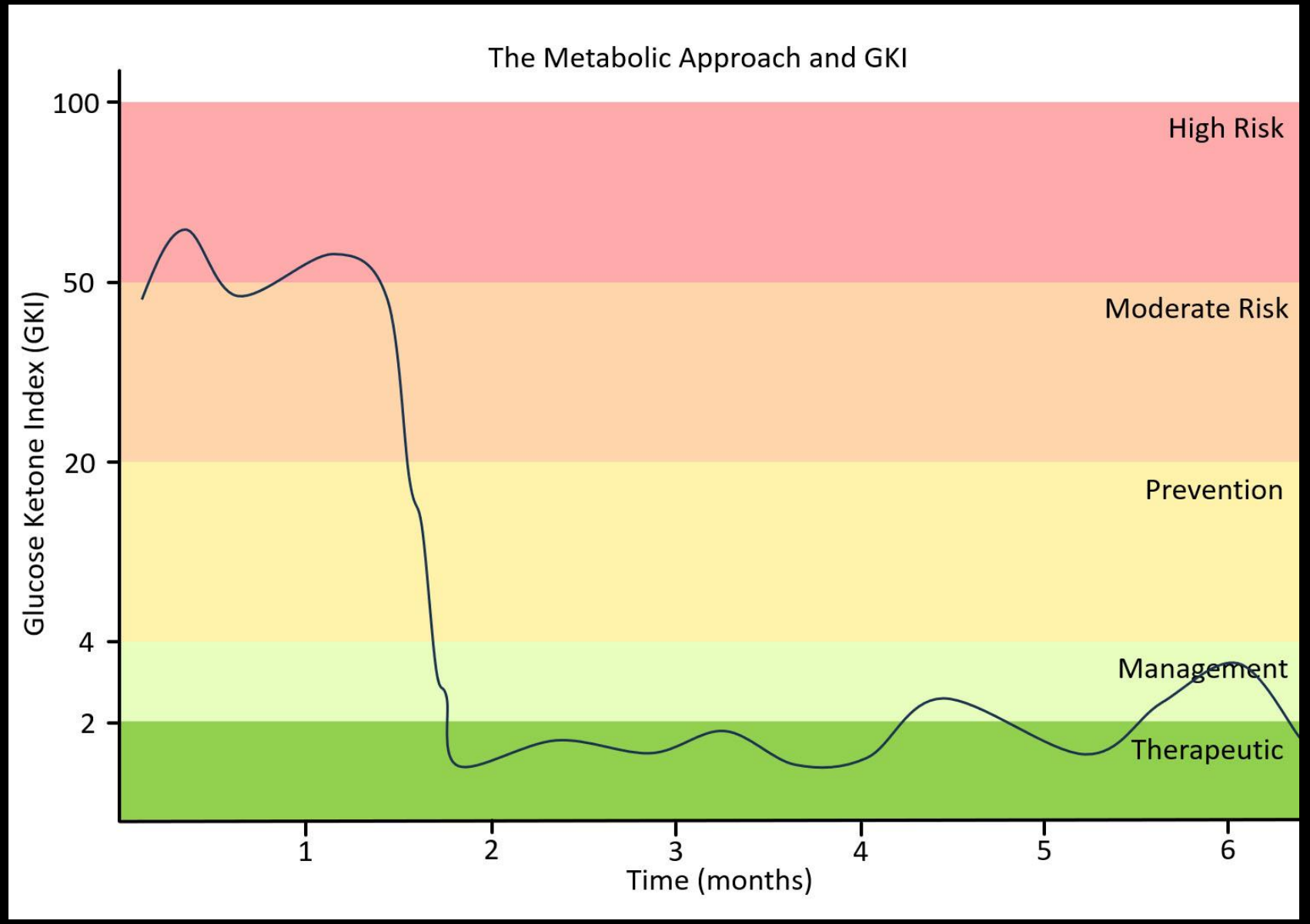
The Glucose Ketone Index (GKI)

The reason as to why it’s now for the metabolic approach

Keto-Mojo



Glucose Ketone Index



Glucose Ketone Index

60

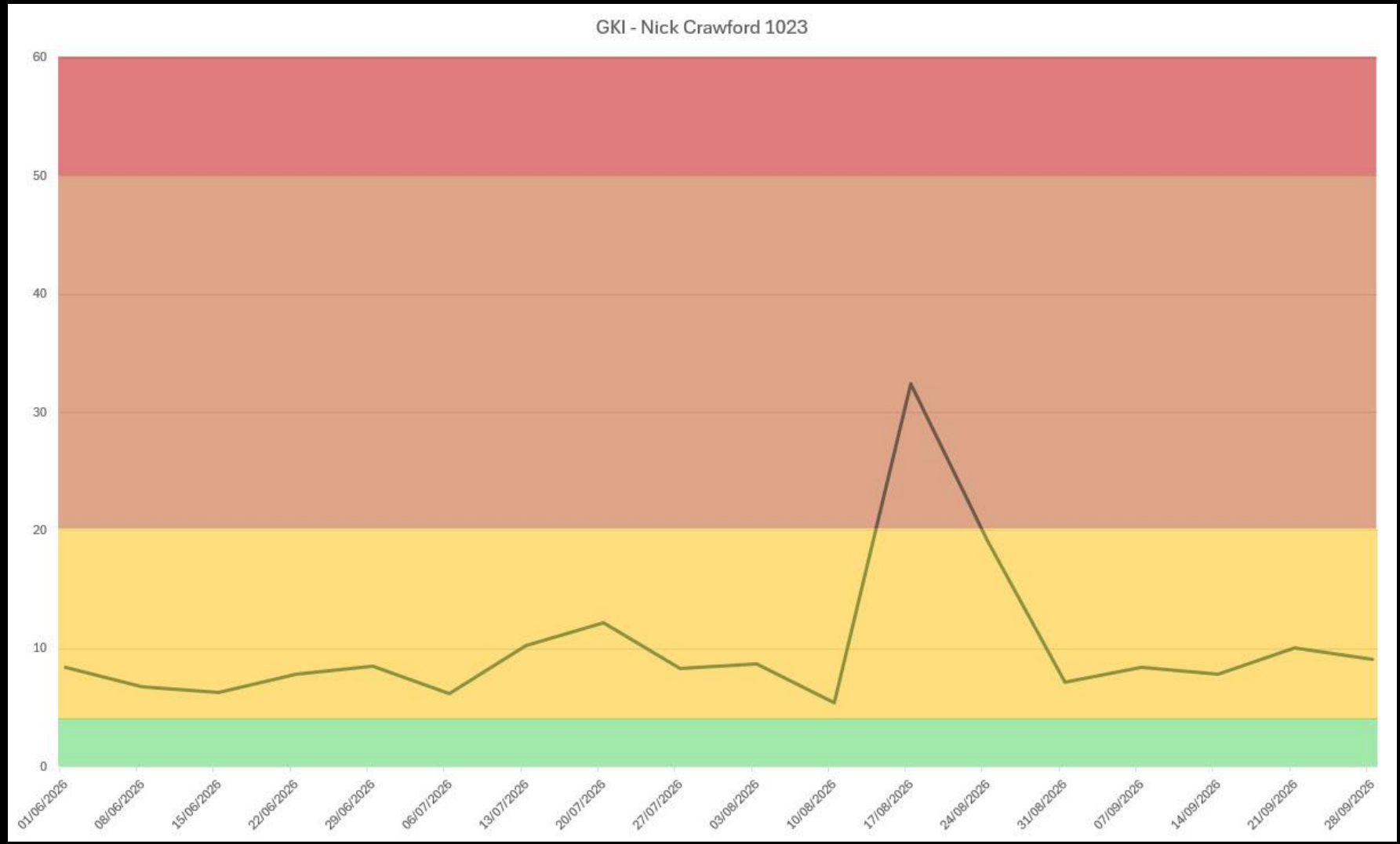
50

40

30

20

10



June 2026

September 2026

Body Composition

Monitoring your body statistics and cachexia

SECA Whole-Body Composition Analyser



seca | results of examination

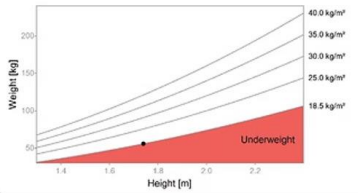
seca Hospital · Dr. John Scotty
Diagnostic Center Cardiology
Hammer Steindamm 9 – 25
22089 Hamburg · Deutschland
+49 40 123456789 · seca@hamburg.com

Patient Data

ID:	12345	Age:	39	Date:	11.11.2014
Name:	Jane Doe	Gender:	Female	Time:	16:20

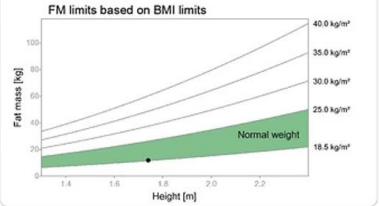
Body Mass Index

Weight: 55.80 kg
Body Mass Index: 18.43 kg/m²
Height: 1.740 m



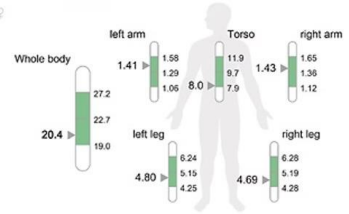
Fat Mass & Fat-Free Mass

Fat Mass (FM): 11.67 kg [20.9 %]*
Fat-Free Mass (FFM): 44.13 kg [79.1 %]*



Skeletal Muscle Mass

Normal range in kg
for 1.740 m

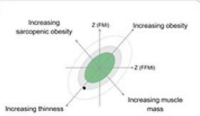


Energy

Resting Energy Expenditure: 924 kcal
Recommended Energy Intake: 1658 kcal
Physical Activity Level: 1.6
Treatment Time: 180 days
Total Energy Expenditure: 1479 kcal
Therapy Goal: 60.00 kg

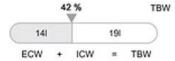
Body Composition Chart

Fat Mass Index (FMI): 3.85 kg/m²
Fat-Free Mass Index (FFMI): 14.58 kg/m²



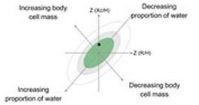
Fluid

Total Body Water (TBW): 32.28 l [57.5 %]*
Extracellular Water (ECW): 13.62 l [24.3 %]*
Hydration (ECW/ICW): 73.0 %



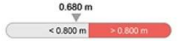
BIVA

Resistance (R): 686.54 Ω
Reactance (Xc): 65.20 Ω



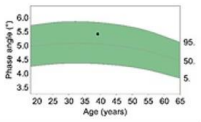
Visceral Adipose Tissue & Waist Circumference

Visceral Adipose Tissue: 0.73 l
Waist Circumference (WC): 0.68 m



Phase Angle

Phase Angle: 5.4°
Percentile: 79.



* percentage of body weight

page 1 | single measurement | © 2014 printout | 09.12.2014

Equipment for Remote Operation

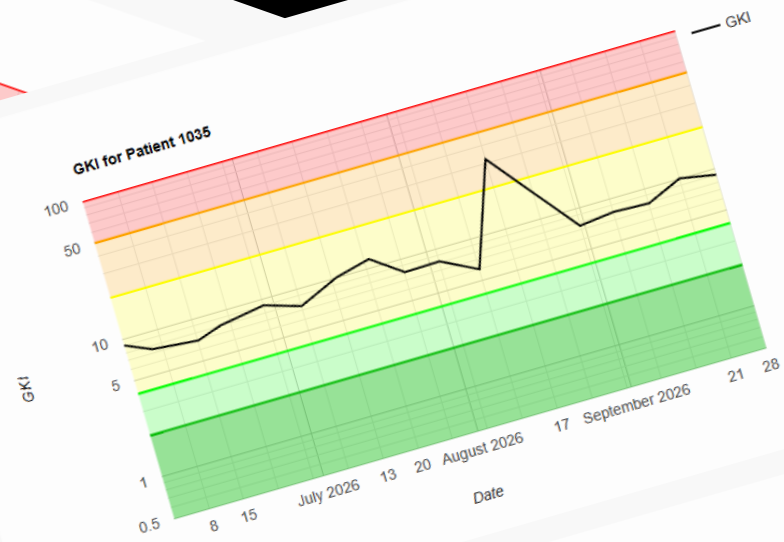


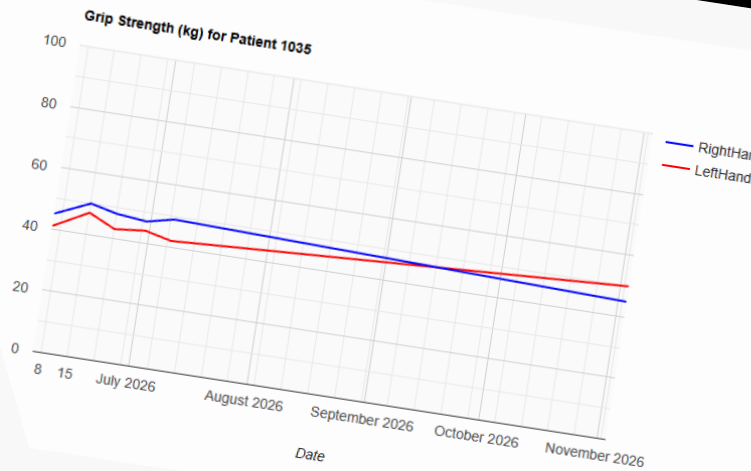
Online Charts



BMI :
Date:

Submit BMI





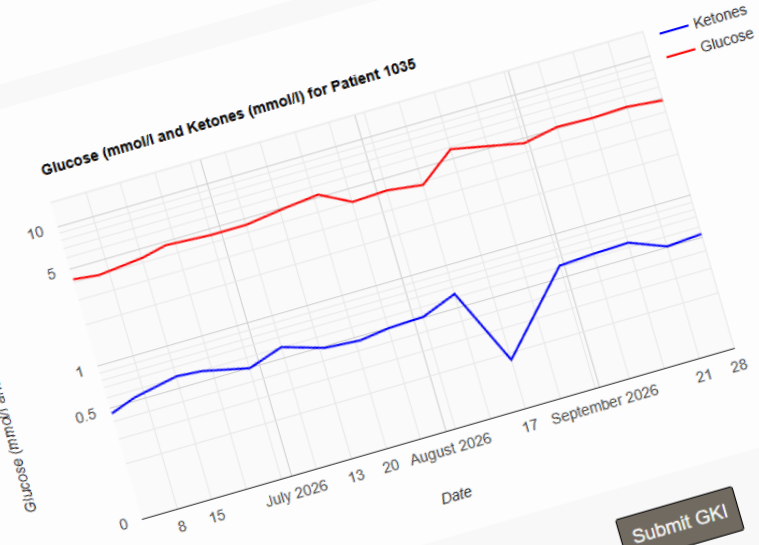
Hand Grip (kg):
nd Grip (kg):
Date:

Submit Grip Results



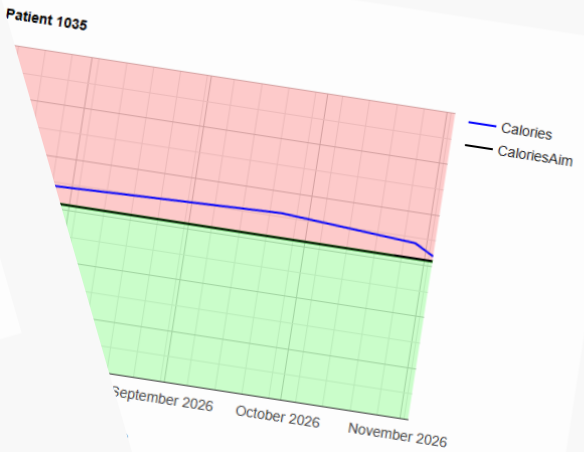
ass %:
ate:

Submit Muscle Ma



GKI :
Glucose (mmol/l):
Ketones (mmol/l):
Date:

Submit GKI



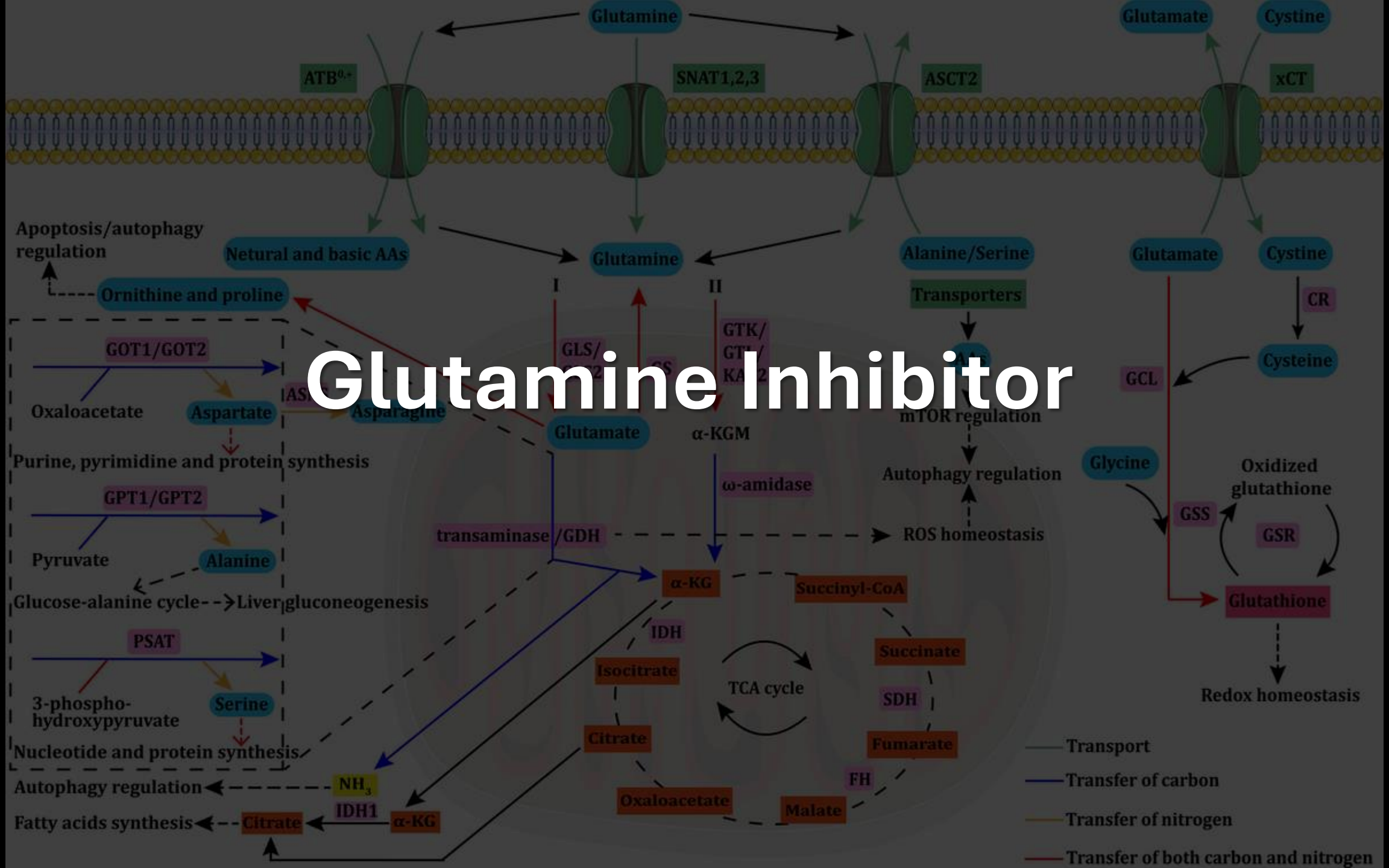
ate:

Submit Calorie Intake

THE METABOLIC APPROACH

STAGE 2

PULSE



Glutamine Inhibitor



Glutamine Inhibitor

THE METABOLIC APPROACH

STAGE 3

THE FINAL INSULT



SEND IN THE SAS

HYPERBARIC OXYGEN THERAPY



HYPERBARIC OXYGEN THERAPY





HYPERBARIC OXYGEN THERAPY





HYPERBARIC OXYGEN THERAPY







HYPERBARIC OXYGEN THERAPY









HYPERBARIC OXYGEN THERAPY









HYPERBARIC OXYGEN THERAPY





SANITY CHECK 3

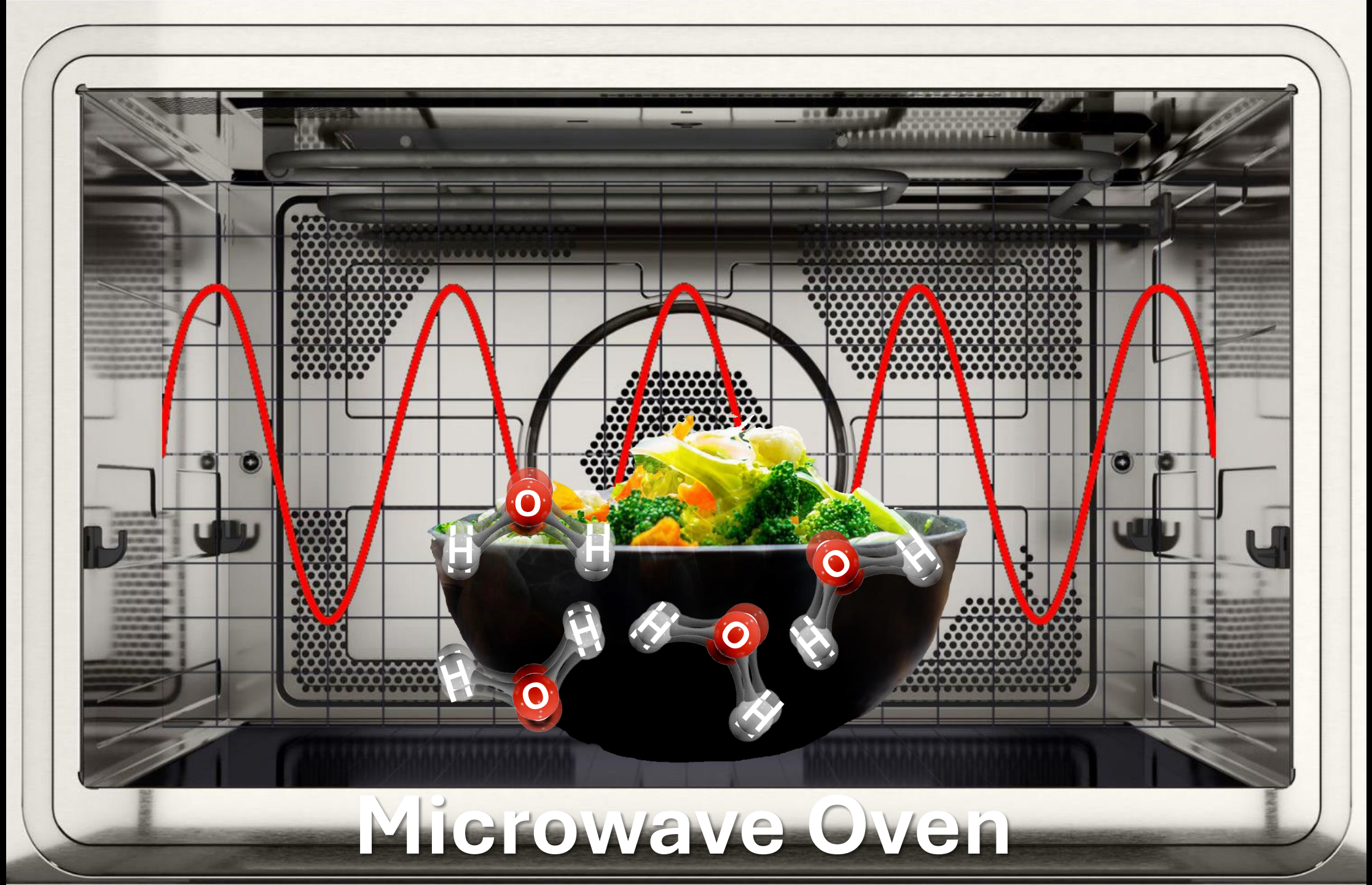
Modern medicine makes use of reactive oxygen species in cancer treatment!



Radiotherapy



Radiation



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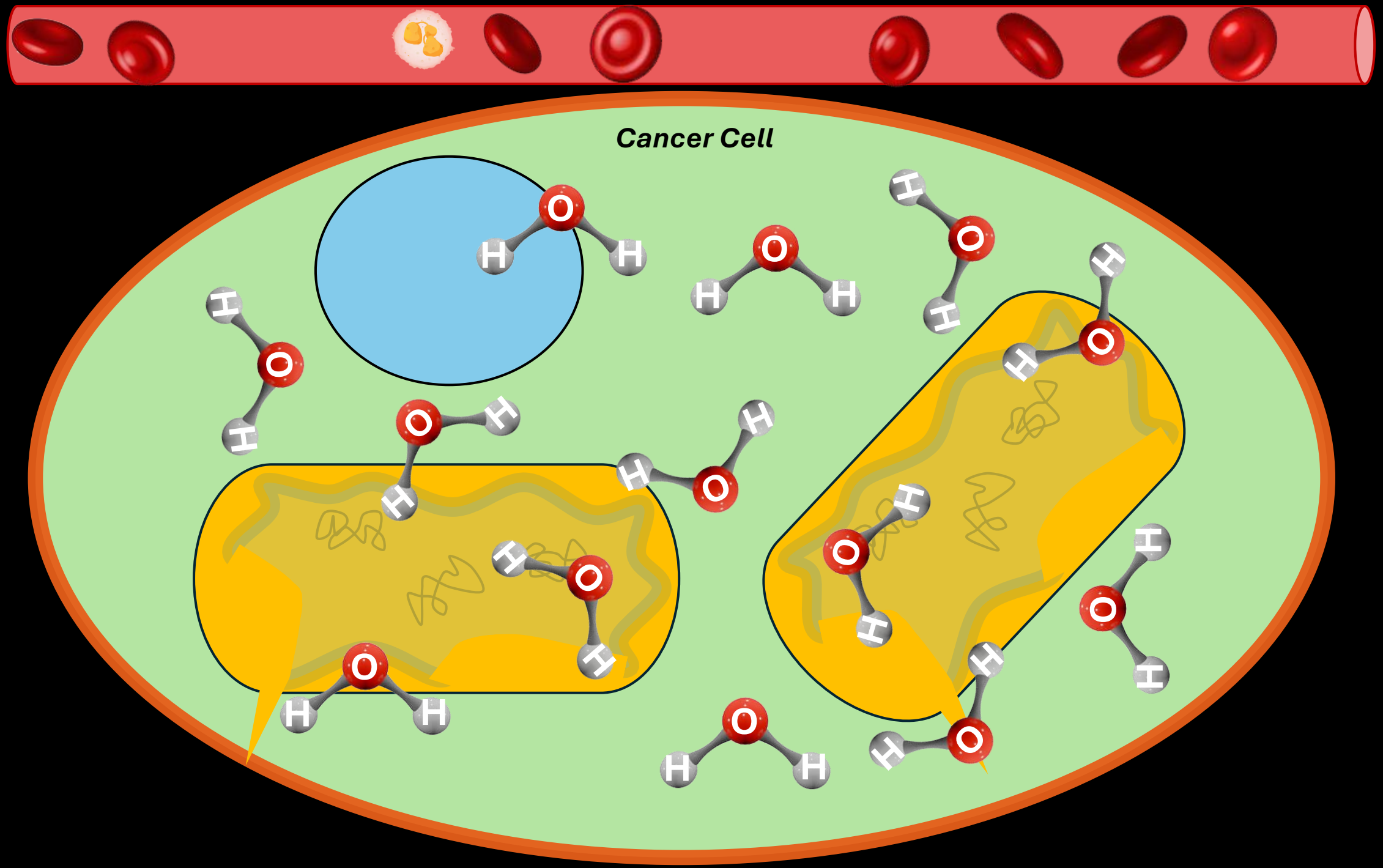
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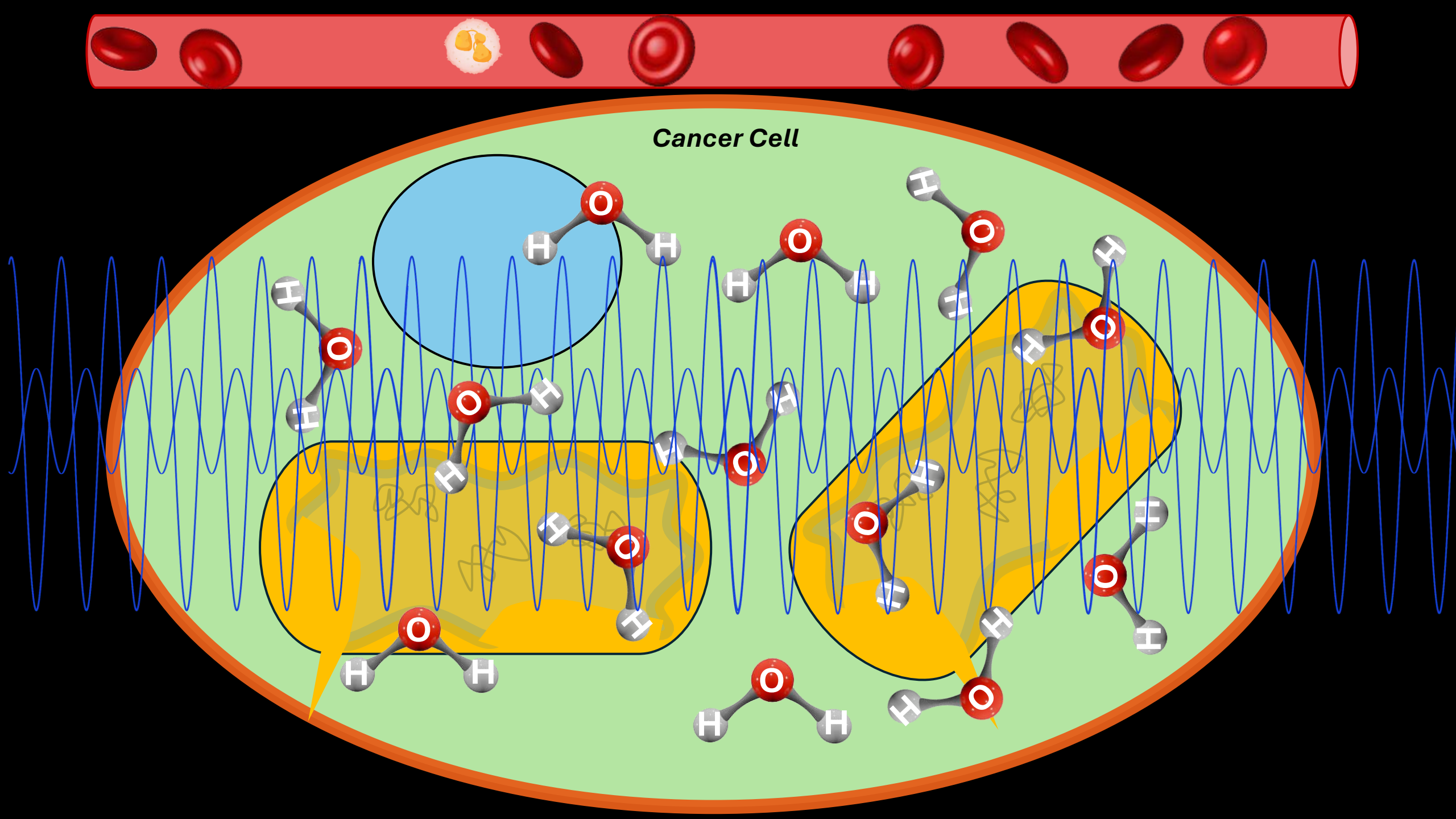
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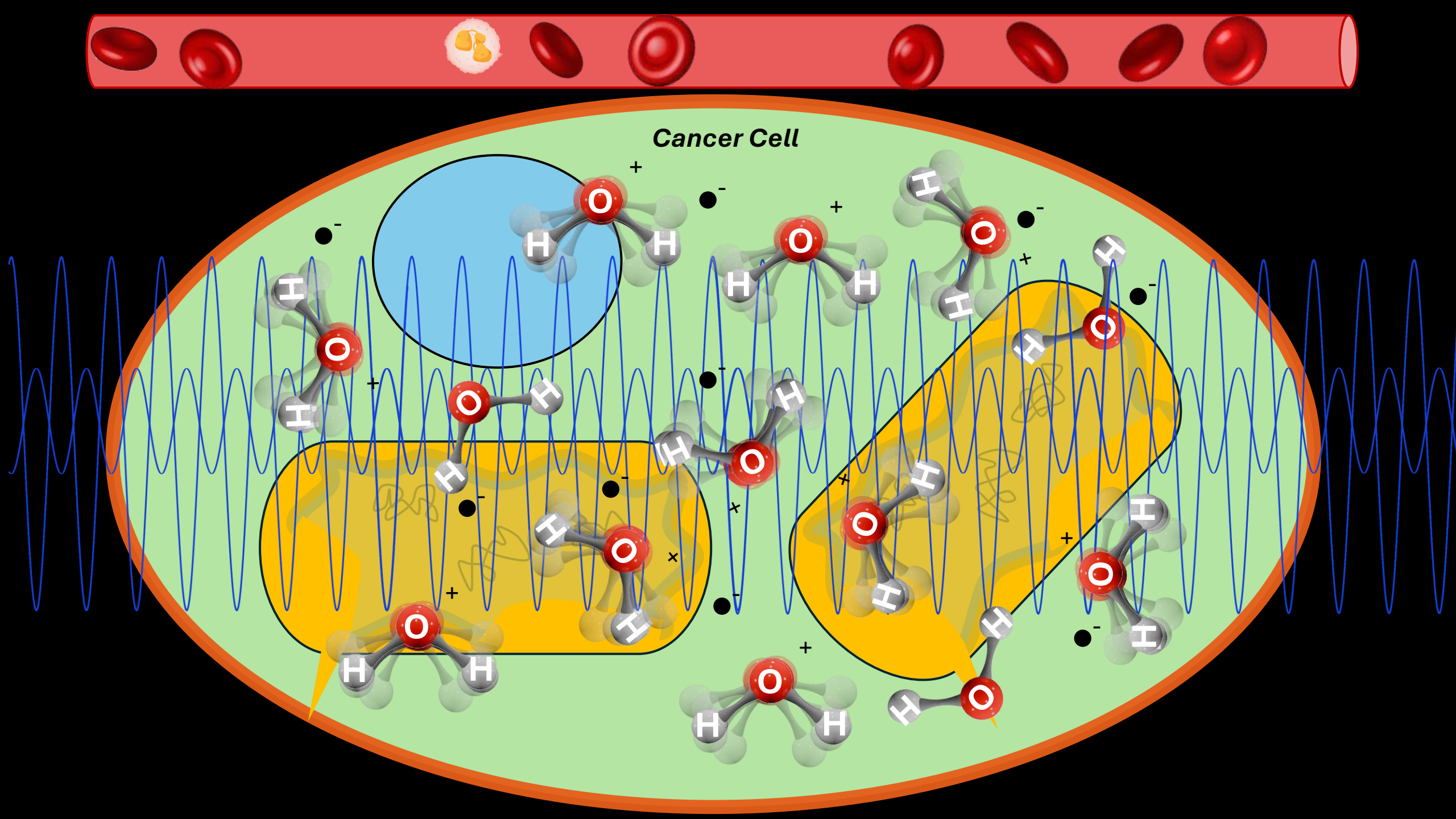
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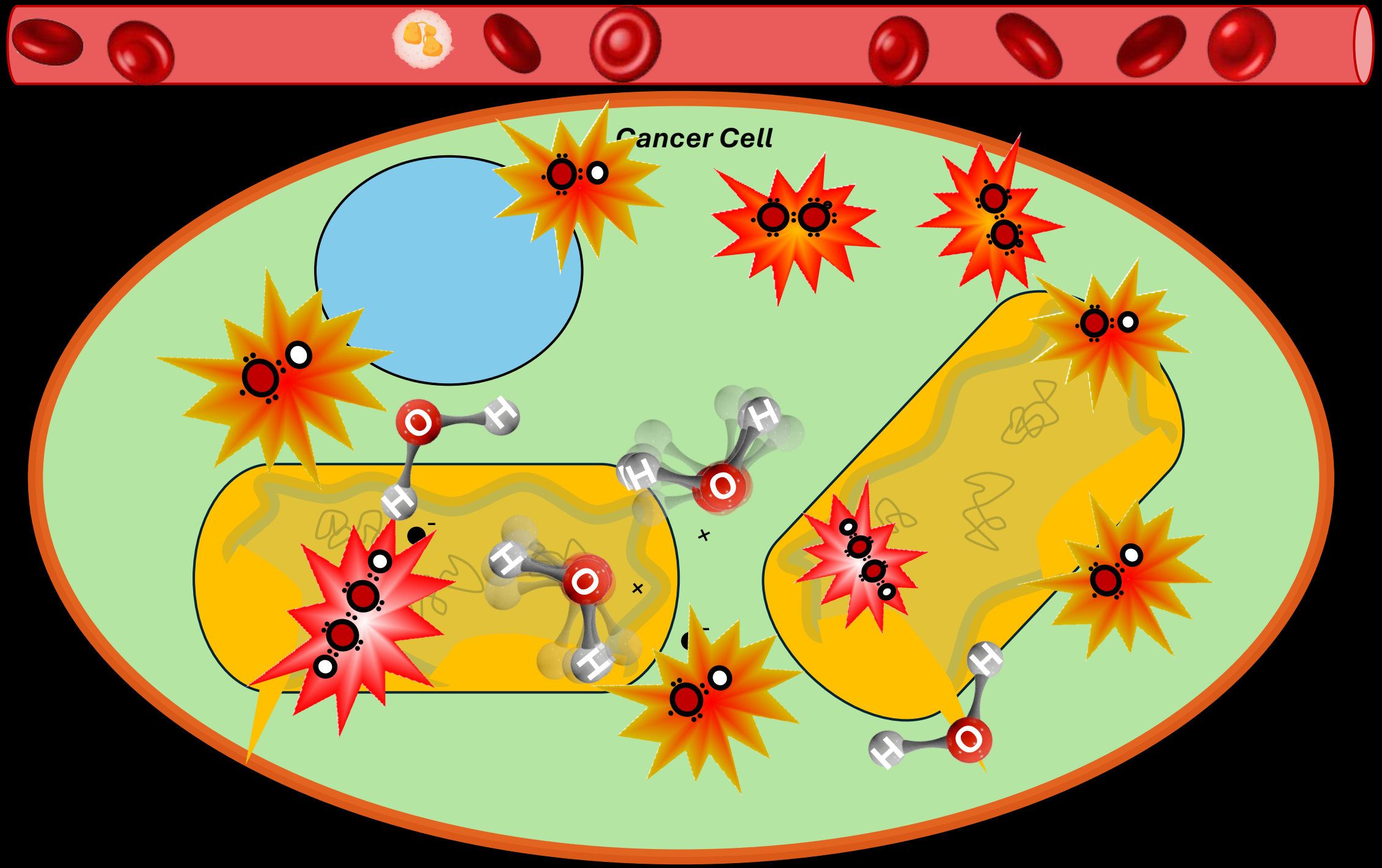
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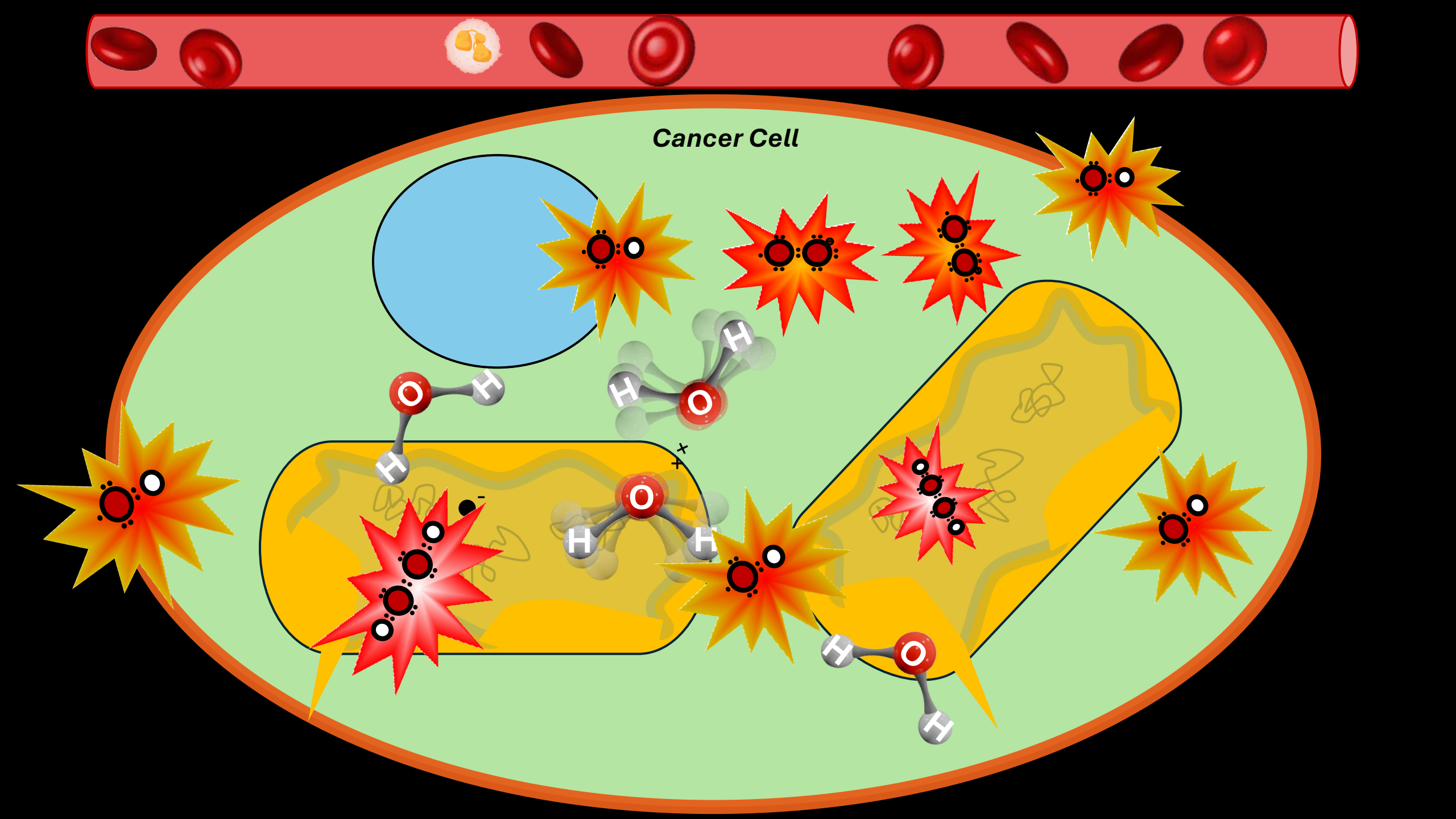
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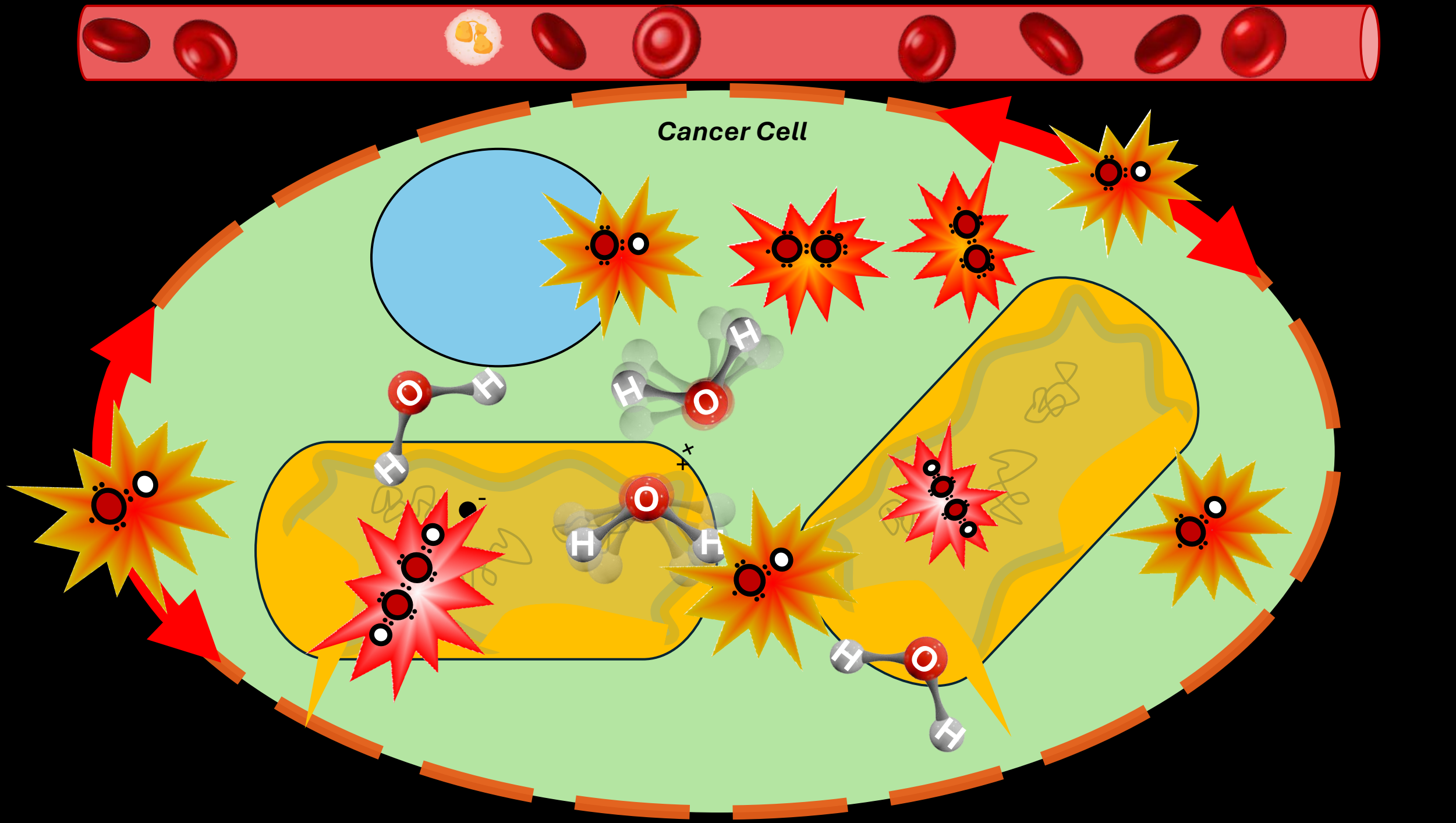
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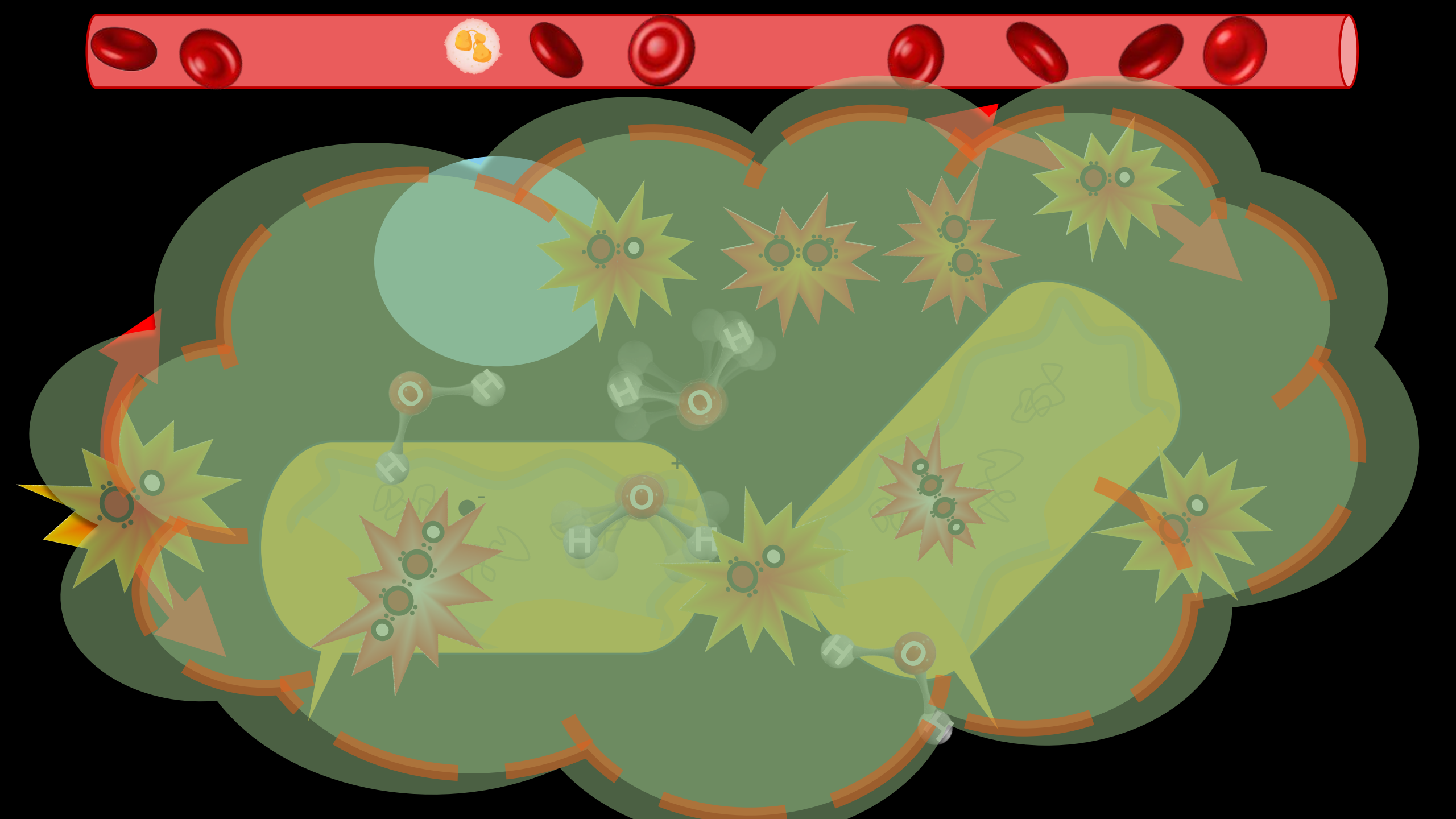
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The Metabolic Approach



The Metabolic Approach

1. Thorough assessment of your condition.

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2. Water-only fasting period, usually for two or three days.

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7. Intensive element would last one to two months.
8. Maintenance protocol established.

The Metabolic Approach

Completely non-toxic

The Metabolic Approach

The Metabolic Approach is not a standalone solution.

Works with your current treatments.

olic Approach



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DEBATE

Clinical research framework proposal for ketogenic metabolic therapy in glioblastoma

Tomás Duraj[1*], Miriam Kalamian[2], Giulio Zuccoli[3], Joseph C. Maroon[4], Dominic P. D'Agostino[5], Adrienne C. Scheck[6], Angela Poff[5], Sebastian F. Winter[7], Jethro Hu[8], Rainer J. Klement[9], Alicia Hickson[10], Derek C. Lee[1], Isabella Cooper[11], Barbara Kofler[12], Kenneth A. Schwartz[13], Matthew C. L. Phillips[14,15], Colin E. Champ[16], Beth Zupec-Kania[17], Jocelyn Tan-Shalaby[18], Fabiano M. Serfaty[19,20], Egiroh Omene[21], Gabriel Arismendi-Morillo[22,23], Michael Kiebish[24], Richard Cheng[25], Ahmed M. El-Sakka[26], Axel Pflueger[27], Edward H. Mathews[28], Donese Worden[29], Hanping Shi[30], Raffaele Ivan Cincione[31], Jean Pierre Spinosa[32], Abdul Kadir Slocum[33], Mehmet Salih Iyikesici[34], Atsuo Yanagisawa[35], Geoffrey J. Pilkington[36], Anthony Chaffee[37], Wafaa Abdel-Hadi[38], Amr K. Elsamman[39], Pavel Klein[40], Keisuke Hagihara[41], Zsófia Clemens[42], George W. Yu[43], Athanasios E. Evangeliou[44], Janak K. Nathan[45], Kris Smith[46], David Fortin[47], Jorg Dietrich[7], Purna Mukherjee and Thomas N. Seyfried[1*]

Abstract

Glioblastoma (GBM) is the most aggressive primary brain tumor in adults, with a universally lethal prognosis despite maximal standard therapies. Here, we present a consensus treatment protocol based on the metabolic requirements of GBM cells for the two major fermentable fuels: glucose and glutamine. Glucose is a source of carbon and ATP synthesis for tumor growth through glycolysis, while glutamine provides nitrogen, carbon, and ATP synthesis through glutaminolysis. As no tumor can grow without anabolic substrates or energy, the simultaneous targeting of glycolysis and glutaminolysis is expected to reduce the proliferation of most if not all GBM cells. Ketogenic metabolic therapy (KMT) leverages diet-drug combinations that inhibit glycolysis, glutaminolysis, and growth signaling while shifting energy metabolism to therapeutic ketosis. The glucose-ketone index (GKI) is a standardized biomarker for assessing biological compliance, ideally via real-time monitoring. KMT aims to increase substrate competition and normalize the tumor microenvironment through GKI-adjusted ketogenic diets, calorie restriction, and fasting, while also targeting glycolytic and glutaminolytic flux using specific metabolic inhibitors. Non-fermentable fuels, such as ketone bodies, fatty acids, or lactate, are comparatively less efficient in supporting the long-term bioenergetic and biosynthetic demands of cancer cell proliferation. The proposed strategy may be implemented as a synergistic metabolic priming baseline in GBM as well as other tumors driven by glycolysis and glutaminolysis, regardless of their residual mitochondrial function. Suggested best practices are provided to guide future KMT research in metabolic oncology, offering a shared, evidence-driven framework for observational and interventional studies.

Keywords Cancer, Glioblastoma, Metabolism, Research design, Warburg Effect, Glutaminolysis, Precision medicine

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Keywords Cancer, Glioblastoma, Metabolism, Research design, Warburg Effect, Glutaminolysis, Precision medi

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Literature Review

Metabolic Therapy as an Adjunct to Conventional Cancer Treatment: A Targeted Approach

Madhu Bala[1], Jyoti Kaur[2]

[1]Assistant Professor, Deptt of Zoology and Environmental Sciences, Punjabi University Patiala Punjab (India), [2]MSc student, Deptt of Zoology and Environmental Sciences, Punjabi University Patiala Punjab (India)

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Abstract

Context: Metabolic therapy encompasses a range of strategies that involve the utilization of metabolic inhibitors, dietary interventions, and natural compounds that modulate metabolic regulators. These methodologies exhibit promising outcomes in preclinical models and early-phase clinical trials for cancer treatment.

Objectives: To elucidate how metabolic therapy disrupts energy production in neoplastic cells while protecting normal cells.

Methods: A comprehensive literature review was conducted utilizing scientific databases.

Results: Metabolic therapy targets cancer cells' energy pathways with inhibitors like metformin and dichloroacetate, disrupting growth without harming normal cells. Dietary strategies, including the ketogenic diet, starve cancer cells and promote fat consumption. Natural compounds like curcumin and resveratrol regulate metabolic processes in cancer cells, potentially slowing tumor growth.

Discussion: Clinical trials have demonstrated encouraging outcomes with the implementation of metabolic therapies.

Conclusion: Strategic exploitation of metabolic vulnerabilities in cancer cells offers a promising avenue for effective therapeutic interventions in the battle against cancer.

Keywords: Metabolic therapy; metabolic inhibitors; dietary interventions; natural compounds; metabolic regulators.

Introduction

Cancer is a malignancy marked by uncontrolled cell growth. It is a leading global cause of death. In the U.S., One in four deaths in 2012 was due to cancer. Worldwide, cancer deaths are expected to rise to 13.2 million by 2030, mainly due to aging and

Corresponding Author: Madhu Bala, Assistant Professor, Deptt of Zoology and Environmental Sciences, Punjabi University Patiala Punjab (India).

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Review

Metabolic Therapy in Glioblastoma—Mapping the Evidence for Ketogenic Diet as an Adjunctive Strategy

Dominika Wiśniewska [1], Martyna Winiarska [1] and Sabina Krupa-Nurcek [2,*]

1 Faculty of Medicine, Collegium Medicum, University of Rzeszów, 35-310 Rzeszow, Poland; dominika.wisniewska.001@gmail.com (D.W.); martynawiniarska44@gmail.com (M.W.)
2 Department of Surgery, Faculty of Medicine, Collegium Medicum, University of Rzeszów, 35-310 Rzeszow, Poland
* Correspondence: sabinakrupa@o2.pl

Abstract

Background/Objectives: Glioblastoma multiforme (GB) is an extremely aggressive tumor of the central nervous system, characterized by rapid growth, high invasiveness, and significant resistance to treatment. A growing body of data indicates that metabolic reprogramming of GB cells may be a therapeutic target, and that the ketogenic diet (KD)—by limiting glucose and inducing ketosis—may modulate tumor metabolism. The aim of this review was to provide a synthetic presentation of the current state of knowledge regarding the use of KD as an adjunctive therapy in the treatment of GB, with a particular focus on the mechanisms of action, safety, feasibility and results of clinical trials. **Methods**: The review was conducted in accordance with the Joanna Briggs Institute methodology and the PRISMA-ScR guidelines. A systematic search of PubMed, Scopus, EBSCO, Web of Science, Google Scholar, and Cochrane Library (1–10 April 2026) included studies on the use of KD in patients with GB. Full-text observational studies, randomised trials and reviews were included in the analysis. Data extraction was carried out according to the Population–Concept–Context (PCC) model. **Results**: Of the 26 publications identified, 12 met the inclusion criteria. Preclinical data consistently indicate that KD may reduce glycolysis, lower insulin and IGF-1 levels, increase oxidative stress in cancer cells, and modulate the inflammatory microenvironment. Clinical trials confirm the safety and feasibility of KD, as well as the ability to maintain stable ketosis. Preliminary data suggest potential metabolic benefits and improved quality of life, however, clinical efficacy remains inconclusive due to small trials, heterogeneous dietary protocols, and a lack of randomized trials. The variety of interventions used (classic KD; MCT-KD-Medium-chain triglyceride KD; KD-IF—KD and intermittent fasting) makes it difficult to compare the results. **Conclusions**: The KD represents a promising, low-toxic strategy to support the treatment of GB, based on biological basis. Available data indicate its safety and feasibility, but there is insufficient evidence to recommend its routine use in clinical practice. Large, multicenter, randomized trials with standardized dietary protocols and objective monitoring of metabolic parameters are needed to unambiguously assess the impact of KD on disease survival and progression.

Keywords: glioblastoma; KD; ketosis; tumor metabolism; neuroinflammation; glucose-ketone index; adjunctive therapy

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METHODOLOGY

Nutrition & Metabolism

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Press-pulse: a novel therapeutic strategy for the metabolic management of cancer

Thomas N. Seyfried[1]*, George Yu[2], Joseph C. Maroon[3] and Dominic P. D'Agostino[4]

Abstract

Background: A shift from respiration to fermentation is a common metabolic hallmark of cancer cells. As a result, glucose and glutamine become the prime fuels for driving the dysregulated growth of tumors. The simultaneous occurrence of "Press-Pulse" disturbances was considered the mechanism responsible for reduction of organic populations during prior evolutionary epochs. Press disturbances produce chronic stress, while pulse disturbances produce acute stress on populations. It was only when both disturbances coincide that population reduction occurred.

Methods: This general concept can be applied to the management of cancer by creating chronic metabolic stresses on tumor cell energy metabolism (press disturbance) that are coupled to a series of acute metabolic stressors that restrict glucose and glutamine availability while also stimulating cancer-specific oxidative stress (pulse disturbances). The elevation of non-fermentable ketone bodies protect normal cells from energy stress while further enhancing energy stress in tumor cells that lack the metabolic flexibility to use ketones as an efficient energy source. Mitochondrial abnormalities and genetic mutations make tumor cells vulnerable metabolic stress.

...esults: The press-pulse therapeutic strategy for cancer management is illustrated with calorie restricted ketogenic ...ets (KD-R) used together with drugs and procedures that create both chronic and intermittent acute stress on ...mor cell energy metabolism, while protecting and enhancing the energy metabolism of normal cells.

...nclusions: Optimization of dosing, timing, and scheduling of the press-pulse therapeutic strategy will facilitate ...eradication of tumor cells with minimal patient toxicity. This therapeutic strategy can be used as a framework ...he design of clinical trials for the non-toxic management of most cancers.

...ords: Glucose, Glutamine, Mitochondria, KETONE bodies, Diet, Warburg effect, Cancer metabolism, ...inolysis, Hyperbaric oxygen

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...to the paleobiologists, Arens and West, the ...us occurrence of "Press-Pulse" disturbances ...dered the mechanism responsible for the ...f organic populations during prior evolution- ...[1]. A "press" disturbance was considered a ...ronmental stress on all organisms in an ...mmunity. The press disturbance promoted ...ough habitat loss, reduced reproduction, ...n of range and resources. Press distur- ...force a biological communi... ...re previously ...

non-viable. A press disturbance would shift the adaptive landscape to favor the fittest species while eliminating the weakest species. In contrast to the press disturbances, "pulse" disturbances were considered acute events that disrupted biological communities to produce high mortality [1]. Through extensive mortality in immediate aftermath of the event ... could cause extinction ... species ...

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Seyfried et al. Nutrition & Metabolism (2017) 14:19
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METHODOLOGY

Nutrition & Metabolism

Open Access

Press-pulse: a novel therapeutic strategy for the metabolic management of cancer

Thomas N. Seyfried[1]*, George Yu[2], Joseph C. Maroon[3] and Dominic P. D'Agostino[4]

Abstract

Background: A shift from respiration to fermentation is a common metabolic hallmark of cancer cells. As a result, glucose and glutamine become the prime fuels for driving the dysregulated growth of tumors. The simultaneous occurrence of "Press-Pulse" disturbances was considered the mechanism responsible for reduction of organic populations during prior evolutionary epochs. Press disturbances produce chronic stress, while pulse disturbances produce acute stress on populations. It was only when both disturbances coincide that population reduction occurred.

Methods: This general concept can be applied to the management of cancer by creating chronic metabolic stresses on tumor cell energy metabolism (press disturbance) that are coupled to a series of acute metabolic stressors that restrict glucose and glutamine availability while also stimulating cancer-specific oxidative stress (pulse disturbances). The elevation of non-fermentable ketone bodies protect normal cells from energy stress while further enhancing energy stress in tumor cells that lack the metabolic flexibility to use ketones as an efficient energy source. Mitochondrial abnormalities and genetic mutations make tumor cells vulnerable metabolic stress.

Results: The press-pulse therapeutic strategy for cancer management is illustrated with calorie restricted ketogenic diets (KD-R) used together with drugs and procedures that create both chronic and intermittent acute stress on tumor cell energy metabolism, while protecting and enhancing the energy metabolism of normal cells.

Conclusions: Optimization of dosing, timing, and scheduling of the press-pulse therapeutic strategy will facilitate eradication of tumor cells with minimal patient toxicity. This therapeutic strategy can be used as a framework for the design of clinical trials for the non-toxic management of most cancers.

...ords: Glucose, Glutamine, Mitochondria, KETONE bodies, Diet, Warburg effect, Cancer metabolism, ...inolysis, Hyperbaric oxygen

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...g to the paleobiologists, Arens and West, the ...us occurrence of "Press-Pulse" disturbances ...dered the mechanism responsible for the ...f organic populations during prior evolution- [1]. A "press" disturbance was considered a ...ronmental stress on all organisms in an ...mmunity. The press disturbance promoted ...ough habitat loss, reduced reproduction, ... of range and resources. Press distur... ...force a biological commu... ...re previously ... non-viable. A press disturbance would shift the adaptive landscape to favor the fittest species while eliminating the weakest species. In contrast to the press disturbances, "pulse" disturbances were considered acute events that disrupted biological communities to produce high mortality [1]. Through extensive mortality in the immediate aftermath of the event, ... could cause extinction ... species ...

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Review

Metabolic Therapy in Glioblastoma—Mapping the Evidence for Ketogenic Diet as an Adjunctive Strategy

Dominika Wiśniewska [1], Martyna Winiarska [1] and Sabina Krupa-Nurcek [2,*]

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35-310 Rzeszow, Poland
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Abstract

Background/Objectives: Glioblastoma multi... of the central nervous system, characterize... significant resistance to treatment. A growin... gramming of GB cells may be a therapeutic ... limiting glucose and inducing ketosis—may ... review was to provide a synthetic presentatio... the use of KD as an adjunctive therapy in t... on the mechanisms of action, safety, feasibi... The review was conducted in accordance wi... and the PRISMA-ScR guidelines. A systema... of Science, Google Scholar, and Cochrane Li... the use of KD in patients with GB. Full-text o... reviews were included in the analysis. Data ... Population–Concept–Context (PCC) model. ... 12 met the inclusion criteria. Preclinical data ... glycolysis, lower insulin and IGF-1 levels, incr... ulate the inflammatory microenvironment. Cl... of KD, as well as the ability to maintain stable ... metabolic benefits and improved quality of life ... sive due to small trials, heterogeneous dietary ... The variety of interventions used (classic KD ... KD-IF—KD and intermittent fasting) makes it ... The KD represents a promising, low-toxic str... on biological basis. Available data indicate its ... evidence to recommend its routine use in clini... trials with standardized dietary protocols and c... are needed to unambiguously assess the impac...

Keywords: glioblastoma; KD; ketosis; t... glucose-ketone index; adjunctive therapy

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Intensive multimodal ketogenic metabolic therapy in glioblastoma: A clinical trial

Matthew C.L. Phillips, Ziad Thotathil, Nur Azri Bin Haji Mohd Yasin, Charles de Groot, Alvin Tan, Marion Kuper-Hommel, Lee-Ann Creagh, Eric Ji, Nichola Naidoo, Mariska van Essen, Fouzia Ziad, Ben G. Moon, Chris Frampton, and Michael B. Jameson

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Abstract

Background. Glioblastoma (GBM), isocitrate dehydrogenase (IDH)-wildtype, has a median overall survi... months despite standard treatment. Ketogenic metabolic interventions that lower the glucose ketone... may improve outcomes. We evaluated the feasibility, tolerability, and potential clinical benefit of integrat... treatment with an intensive multimodal metabolic therapy program (MTP) in newly diagnosed IDH-wi...

Methods. Patients received standard chemoradiation and adjuvant chemotherapy alongside an MT... prolonged fasting, time-restricted feeding, and a ketogenic diet. The primary outcome was the proport... a mean daily GKI ≤6 during chemoradiation. Secondary outcomes included GKI control throughout c... body weight, body mass index, adverse events, performance, exercise, quality of life, and survival, ... contemporary controls using unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs).

Results. Among 32 eligible patients, 18 commenced chemoradiation with the MTP (intention-to-trea... pleted it (per-protocol). In the intention-to-treat population, 15 of 18 patients (83%) sustained a me... during chemoradiation. Among per-protocol patients, the GKI was 1.88 ± 0.56 during chemoradiatio... throughout chemotherapy. Intentional weight loss averaged 17%, normalizing body mass index. MT... events were mild or moderate. Exercise activity and quality of life improved. Median overall survival... versus 14.7 months in controls (HR = 0.42, 95% CI 0.18-0.97, $P = .027$), with 3-year survival of 27% ...

Conclusions. Intensive multimodal metabolic therapy was feasible, well-tolerated, and associat... exercise activity, quality of life, and survival outcomes, including higher 3-year survival.

Key Points

- The MTP was feasible, well-tolerated, and had high completion rates.
- Patients sustained a low GKI, with improved exercise activity and quality of life.
- Survival was greater—median 21.5 versus 14.7 months, 3-year 27% versus 7%.

...the most common primary malignant ... treatment challenges due ... adjuvant temozolomide chemothe... cally yielding a median overall ... Classification based on isocitrate d... further refined the G...



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Article

Promising Effect of a New Ketogenic Diet Regimen in Patients with Advanced Cancer

Keisuke Hagihara [1,*], Katsufumi Kajimoto [1], Satoshi Osaga [2], Naoko Nagai [3], Eku Shimosegawa [4], Hideyuki Nakata [1], Hitomi Saito [1], Mai Nakano [1], Mariko Takeuchi [1], Hideaki Kanki [1], Kuriko Kagitani-Shimono [5] and Takashi Kijima [6]

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Abstract: A ketogenic diet is expected to be an effective support therapy for patients with cancer, but the degree and duration of carbohydrate restriction are unclear. We performed a case series study of a new ketogenic diet regimen in patients with different types of stage IV cancer. Carbohydrates were restricted to 10 g/day during week one, 20 g/day from week two for three months, and 30 g/day thereafter. A total of 55 patients participated in the study, and data from 37 patients administered the ketogenic diet for three months were analyzed. No severe adverse events associated with the diet were observed. Total ketone bodies increased significantly, and both fasting blood sugar and insulin levels were suppressed significantly for three months after completion of the study. Five patients showed a partial response on Positron emission tomography–computed tomography (PET-CT) at three months. Three and seven patients showed complete and partial responses, respectively at one year. Median survival was 32.2 (maximum: 80.1) months, and the three-year survival rate was 44.5%. After three months on the ketogenic diet, the serum Alb, BS, and CRP (ABC) score could be used to stratify the patients into groups with significantly different survival rates ($p < 0.001$, log-rank

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Intensive multimodal ketogenic metabolic therapy in glioblastoma: A clinical trial

Matthew C.L. Phillips, Ziad Thotathil, Nur Azri Bin Haji Mohd Yasin, Charles de Groot, Alvin Tan, Marion Kuper-Hommel, Lee-Ann Creagh, Eric Ji, Nichola Naidoo, Mariska van Essen, Fouzia Ziad, Ben G. Moon, Chris Frampton, and Michael B. Jameson

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Corresponding Author: Matthew C.L. Phillips, FRACP, Department of Neurology, Waikato Hospital, Hamilton 3204, New Zealand (Matthew.Phillips@waikatodhb.health.nz).

Abstract

Background. Glioblastoma (GBM), isocitrate dehydrogenase (IDH)-wildtype, has a median overall survival of 15 months despite standard treatment. Ketogenic metabolic interventions that lower the glucose ketone index may improve outcomes. We evaluated the feasibility, tolerability, and potential clinical benefit of integrating ketogenic metabolic therapy with an intensive multimodal metabolic therapy program (MTP) in newly diagnosed IDH-wildtype GBM.

Methods. Patients received standard chemoradiation and adjuvant chemotherapy alongside an MTP including prolonged fasting, time-restricted feeding, and a ketogenic diet. The primary outcome was the proportion achieving a mean daily GKI ≤6 during chemoradiation. Secondary outcomes included GKI control throughout chemotherapy, body weight, body mass index, adverse events, performance, exercise, quality of life, and survival, compared with contemporary controls using unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs).

Results. Among 32 eligible patients, 18 commenced chemoradiation with the MTP (intention-to-treat) and 15 completed it (per-protocol). In the intention-to-treat population, 15 of 18 patients (83%) sustained a mean GKI ≤6 during chemoradiation. Among per-protocol patients, the GKI was 1.88 ± 0.56 during chemoradiation and throughout chemotherapy. Intentional weight loss averaged 17%, normalizing body mass index. MTP-related events were mild or moderate. Exercise activity and quality of life improved. Median overall survival was 21.5 versus 14.7 months in controls (HR = 0.42, 95% CI 0.18-0.97, $P = .027$), with 3-year survival of 27% versus 7%.

Conclusions. Intensive multimodal metabolic therapy was feasible, well-tolerated, and associated with improved exercise activity, quality of life, and survival outcomes, including higher 3-year survival.

Key Points

- The MTP was feasible, well-tolerated, and had high completion rates.
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Article

Promising Effect of a New Ketogenic Diet Regimen in Patients with Advanced Cancer

Keisuke Hagihara [1,*], Katsufumi Kajimoto [1], Satoshi Osaga [2], Naoko Nagai [3], Eku Shimosegawa [4], Hideyuki Nakata [1], Hitomi Saito [1], Mai Nakano [1], Mariko Takeuchi [1], Hideaki Kanki [1], Kuriko Kagitani-Shimono [5] and Takashi Kijima [6]

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Received: 22 April 2020; Accepted: 15 May 2020; Published: 19

Abstract: A ketogenic diet is expected to be an effective s the degree and duration of carbohydrate restriction are of a new ketogenic diet regimen in patients with differe were restricted to 10 g/day during week one, 20 g/day fr thereafter. A total of 55 patients participated in the study ketogenic diet for three months were analyzed. No se were observed. Total ketone bodies increased significan levels were suppressed significantly for three months showed a partial response on Positron emission tomo three months. Three and seven patients showed co one year. Median survival was 32.2 (maximum: 80.1) 44.5%. After three months on the ketogenic diet, the s used to stratify the patients into groups with significa

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Intensive multimodal ketogenic metabolic therapy in glioblastoma: A clinical trial

Mohd Yasin, Charles de Groot, Alvin Tar Essen, Fouzia Ziad

Original Article

The Glucose Ketone Index predicts overall survival and metastasis of mouse tumor cells to visceral organs and brain

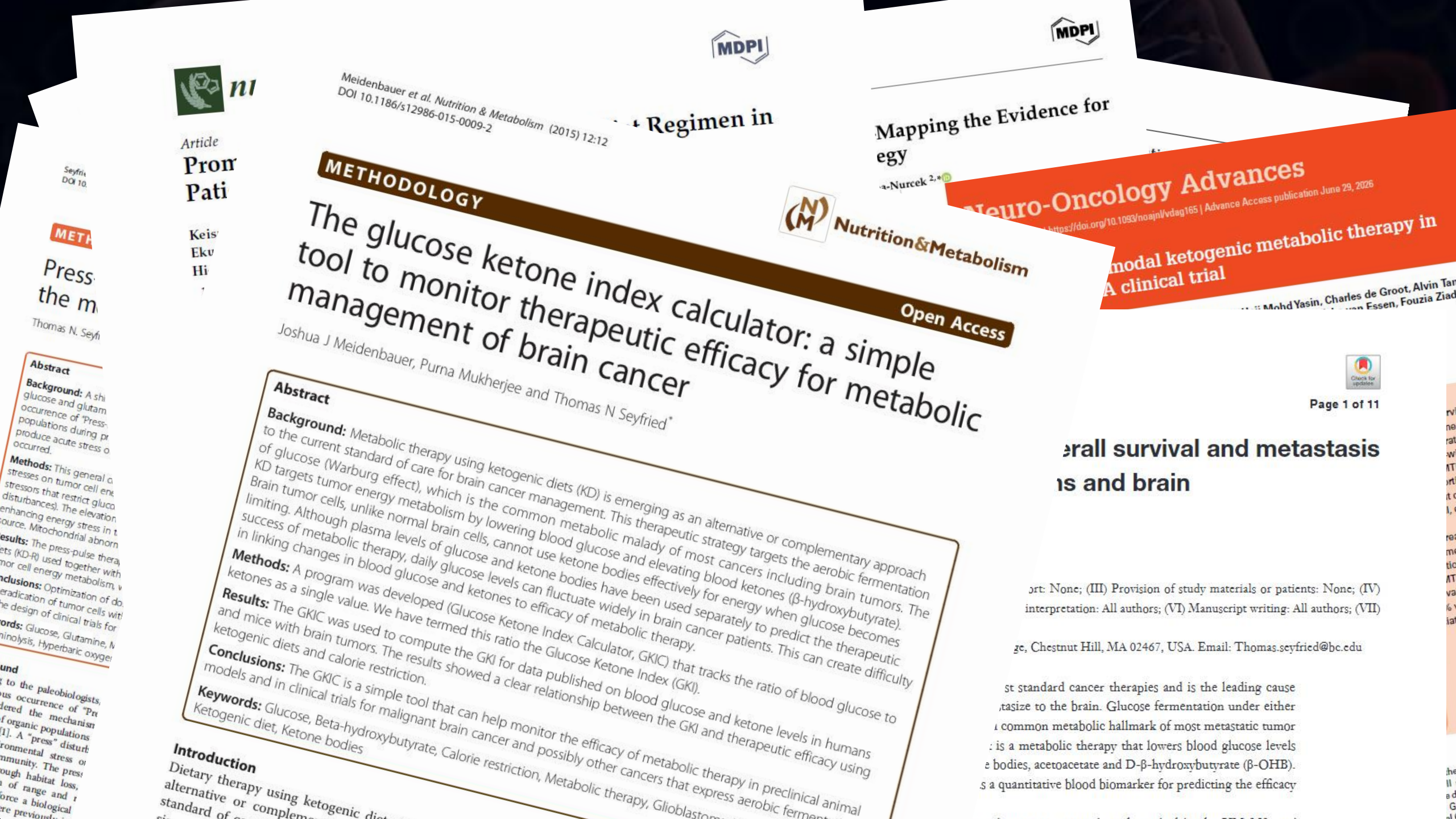
Zeynep Akgoc, Purna Mukherjee, Thomas N. Seyfried^

Department of Biology, Boston College, Chestnut Hill, MA, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: Z Akgoc, P Mukherjee; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Thomas N. Seyfried. Department of Biology, Boston College, Chestnut Hill, MA 02467, USA. Email: Thomas.seyfried@bc.edu

Background: Metastasis is largely refractory to most standard cancer therapies and is the leading cause of cancer death, especially after the tumor cells metastasize to the brain. Glucose fermentation under either anaerobic or aerobic conditions (Warburg Effect) is a common metabolic hallmark of most metastatic tumor cells. The high-fat low carbohydrate ketogenic diet is a metabolic therapy that lowers blood glucose levels while elevating levels of the non-fermentable ketone bodies, acetoacetate and D-β-hydroxybutyrate (β-OHB). The Glucose Ketone Index (GKI) was developed as a quantitative blood biomarker for predicting the efficacy of anti-cancer metabolic therapies.



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Meidenbauer et al. Nutrition & Metabolism (2015) 12:12
DOI 10.1186/s12986-015-0009-2

METHODOLOGY

Open Access

The glucose ketone index calculator: a simple tool to monitor therapeutic efficacy for metabolic management of brain cancer

Joshua J Meidenbauer, Purna Mukherjee and Thomas N Seyfried*

Abstract

Background: Metabolic therapy using ketogenic diets (KD) is emerging as an alternative or complementary approach to the current standard of care for brain cancer management. This therapeutic strategy targets the aerobic fermentation of glucose (Warburg effect), which is the common metabolic malady of most cancers including brain tumors. The KD targets tumor energy metabolism by lowering blood glucose and elevating blood ketones (β-hydroxybutyrate). Brain tumor cells, unlike normal brain cells, cannot use ketone bodies effectively for energy when glucose becomes limiting. Although plasma levels of glucose and ketone bodies have been used separately to predict the therapeutic success of metabolic therapy, daily glucose levels can fluctuate widely in brain cancer patients. This can create difficulty in linking changes in blood glucose and ketones to efficacy of metabolic therapy.

Methods: A program was developed (Glucose Ketone Index Calculator, GKIC) that tracks the ratio of blood glucose to ketones as a single value. We have termed this ratio the Glucose Ketone Index (GKI).

Results: The GKIC was used to compute the GKI for data published on blood glucose and ketone levels in humans and mice with brain tumors. The results showed a clear relationship between the GKI and therapeutic efficacy using ketogenic diets and calorie restriction.

Conclusions: The GKIC is a simple tool that can help monitor the efficacy of metabolic therapy in preclinical animal models and in clinical trials for malignant brain cancer and possibly other cancers that express aerobic ferment

Keywords: Glucose, Beta-hydroxybutyrate, Calorie restriction, Metabolic therapy, Glioblasto
Ketogenic diet, Ketone bodies

Introduction

Dietary therapy using ketogenic diet
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Neuro-Oncology Advances

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Mohd Yasin, Charles de Groot, Alvin Tar
Essen, Fouzia Ziad

Page 1 of 11

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ort: None; (III) Provision of study materials or patients: None; (IV)
interpretation: All authors; (VI) Manuscript writing: All authors; (VII)

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Thomas N. Seyfr

Abstract

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Review

Ketogenic Diet in Cancer Prevention and Therapy: Molecular Targets and Therapeutic Opportunities

Wamidh H. Talib [1,*], Asma Ismail Mahmod [1], Ayah Kamal [1], Hasan M. Rashid [1], Aya M. D. Alashqar [1], Samar Khater [1], Duaa Jamal [1] and Mostafa Waly [2]

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Abstract: Although cancer is still one of the most significant global challenges facing public health, the world still lacks complementary approaches that would significantly enhance the efficacy of standard anticancer therapies. One of the essential strategies during cancer treatment is following a healthy diet program. The ketogenic diet (KD) has recently emerged as a metabolic therapy in cancer treatment, targeting cancer cell metabolism rather than a conventional dietary approach. The ketogenic diet (KD), a high-fat and very-low-carbohydrate with adequate amounts of protein, has shown antitumor effects by reducing energy supplies to cells. This low energy supply inhibits tumor growth, explaining the ketogenic diet's therapeutic mechanisms in cancer treatment. This review highlights the crucial mechanisms that explain the ketogenic diet's potential antitumor effects, which probably produces an unfavorable metabolic environment for cancer cells and can be used as a promising adjuvant in cancer therapy. Studies discussed in this review provide a solid background for researchers and physicians to design new combination therapies based on KD and conventional therapies.

Keywords: alternative cancer therapies; anticancer diet; targeting cancer metabolism; calories restriction

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1. Introduction

Cancer, "the sickness of the century", is one of this era's leading causes of mortality worldwide, which is becoming more threatening day by day due to the increasing number of cancer cases and the ability of this disease to resist the existent therapeutic and pharmacological approaches. In the year 2020 and in the United States alone, 1,806,590 new cancer cases were discovered according to the American Cancer Society, with 606,520 cancer deaths [1]. With approximately 89,500 new cancer cases per year and 9270 deaths in adolescents and young adults [2]. The conventional interventions such as surgery, chemotherapy, hormonal therapy, radiation therapy, monoclonal antibodies, and tyrosine kinase inhibitors were able to eliminate some types of cancers, induce cancer regression and inhibit the growth of some others [3]. Nevertheless, each one of these interventions has its own limitations that can be an obstacle to both healthcare providers and patients to reach the desirable objectives; for example, the advanced stage of cancer and metastasis level renders the surgical procedure unreasonable and not effective. In addition, both chemotherapy and radiation therapy have cancer induction effects that may lead to secondary tumors and various toxicity issues inducing normal-tissue complications; these factors and others put pressure on the medical body to find new, safe, and cost-effective cancer therapy agents [3].

The metabolic differences between normal cells and cancerous cells is not a new subject, especially after the discovery of the Warburg effect by Otto Warburg in 1920s [4–6],

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Meidenbauer et al. Nutrition & Metabolism (2015) 12:12
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Article

METHODOLOGY

The glucose ketone index calculator: a tool to monitor therapeutic efficacy for management of brain cancer

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Results: The GKIC was used to compute the GKI for data published on blood glucose and ketone levels in h and mice with brain tumors. The results showed a clear relationship between the GKI and therapeutic efficacy ketogenic diets and calorie restriction.

Conclusions: The GKIC is a simple tool that can help monitor the efficacy of metabolic therapy in preclinical animal models and in clinical trials for malignant brain cancer and possibly other cancers that express aerobic ferment

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Introduction

Dietary therapy using ketogenic diet
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REVIEW
published: 11 March 2020
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Consideration of Ketogenic Metabolic Therapy as a Complementary or Alternative Approach for Managing Breast Cancer

Thomas N. Seyfried[1]*, Purna Mukherjee[1], Mehmet S. Iyikesici[2], Abdul Slocum[3], Miriam Kalamian[4], Jean-Pierre Spinosa[5] and Christos Chinopoulos[6]

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Sharon Ross,

Breast cancer remains as a significant cause of morbidity and mortality in women. Ultrastructural and biochemical evidence from breast biopsy tissue and cancer cells shows mitochondrial abnormalities that are incompatible with energy production through oxidative phosphorylation (OxPhos). Consequently, breast cancer, like most cancers, will become more reliant on substrate level phosphorylation (fermentation) than on oxidative phosphorylation (OxPhos) for growth consistent with the mitochondrial metabolic theory of cancer. Glucose and glutamine are the prime fermentable fuels that underlie therapy resistance and drive breast cancer growth through substrate level phosphorylation (SLP) in the cytoplasm (Warburg effect) and the mitochondria (Q-effect), respectively. ... indicates that ketogenic metabolic therapy (KMT) can reduce glucose ... simultaneously elevating ketone bodies, a non-fermentable ... would be most effective when used together ... suggesting how KMT could reduce ... damage to normal cells.

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Review

Ketogenic Diet in Cancer Prevention and Therapy: Molecular Targets and Therapeutic Opportunities

Wamidh H. Talib [1,*], Asma Ismail Mahmod [1], Ayah Kamal [1], Hasan M. Rashid [1], Aya M. D. Alashqar [1], Samar Khater [1], Duaa Jamal [1] and Mostafa Waly [2]

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* Correspondence: w_talib@asu.edu.jo

Abstract: Although cancer is still one of the most significant global challenges facing public health, the world still lacks complementary approaches that would significantly enhance the efficacy of standard anticancer therapies. One of the essential strategies during cancer treatment is following a healthy diet program. The ketogenic diet (KD) has recently emerged as a metabolic therapy in cancer treatment, targeting cancer cell metabolism rather than a conventional dietary approach. The ketogenic diet (KD), a high-fat and very-low-carbohydrate with adequate amounts of protein, has shown antitumor effects by reducing energy supplies to cells. This low energy supply inhibits tumor growth, explaining the ketogenic diet's therapeutic mechanisms in cancer treatment. This review highlights the crucial mechanisms that explain the ketogenic diet's potential antitumor effects, which probably produces an unfavorable metabolic environment for cancer cells and can be used as a promising adjuvant in cancer therapy. Studies discussed in this review provide a solid background for researchers and physicians to design new combination therapies based on KD and conventional therapies.

Keywords: alternative cancer therapies; anticancer diet; targeting cancer metabolism; calories restriction

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1. Introduction

Cancer, "the sickness of the century", is one of this era's leading causes of mortality worldwide, which is becoming more threatening day by day due to the increasing number of cancer cases and the ability of this disease to resist the existent therapeutic and pharmacological approaches. In the year 2020 and in the United States alone, 1,806,590 new cancer cases were discovered according to the American Cancer Society, with 606,520 cancer deaths [1]. With approximately 89,500 new cancer cases per year and 9270 deaths in adolescents and young adults [2]. The conventional interventions such as surgery, chemotherapy, hormonal therapy, radiation therapy, monoclonal antibodies, and tyrosine kinase inhibitors were able to eliminate some types of cancers, induce cancer regression and inhibit the growth of some others [3]. Nevertheless, each one of these interventions has its own limitations that can be an obstacle to both healthcare providers and patients to reach the desirable objectives; for example, the advanced stage of cancer and metastasis level renders the surgical procedure unreasonable and not effective. In addition, both chemotherapy and radiation therapy have cancer induction effects that may lead to secondary tumors and various toxicity issues inducing normal-tissue complications; these factors and others put pressure on the medical body to find new, safe, and cost-effective cancer therapy agents [3].

The metabolic differences between normal cells and cancerous cells is not a new subject, especially after the discovery of the Warburg effect by Otto Warburg in 1920s [4–6],



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REVIEW

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The glucose ketone index: a proposed quantitative biomarker to support cancer and chronic disease prevention and management

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Abstract

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Review

Ketogenic Diet in Cancer Prevention and Therapy: Molecular Targets and Therapeutic Opportunities

Wamidh H. Talib [1,*], Asma Ismail Mahmod [1], Ayah Kamal [1], Hasan M. Rashid [1], Aya M. D. Alashqar [1], Samar Khater [1], Duaa Jamal [1] and Mostafa Waly [2]

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Abstract: Although cancer is still one of the most significant global challenges facing public health, the world still lacks complementary approaches that would significantly enhance the efficacy of standard anticancer therapies. One of the essential strategies during cancer treatment is following a healthy diet program. The ketogenic diet (KD) has recently emerged as a metabolic therapy in cancer treatment, targeting cancer cell metabolism rather than a conventional dietary approach. The ketogenic diet (KD), a high-fat and very-low-carbohydrate with adequate amounts of protein, has shown antitumor effects by reducing energy supplies to cells. This low energy supply inhibits tumor growth, explaining the ketogenic diet's therapeutic mechanisms in cancer treatment. This review highlights the crucial mechanisms that explain the ketogenic diet's potential antitumor effects, which probably produces an unfavorable metabolic environment for cancer cells and can be used as a promising adjuvant in cancer therapy. Studies discussed in this review provide a solid background for researchers and physicians to design new combination therapies based on KD and conventional therapies.

Keywords: alternative cancer therapies; anticancer diet; targeting cancer metabolism; calories restriction

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1. Introduction

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The glucose ketone index: a proposed quantitative biomarker to support cancer and chronic disease prevention and management

Derek C. Lee[1*], Tomas Duraj[1], Isabella D. Cooper[2], Joseph C. Maroon[3], Kris Smith[4], Wafaa Abdel-Hadi[5], Egiroh Omene[6], Athanasios E. Evangeliou[7] and Thomas N. Seyfried[1*]

Abstract

The chronic disease burden is rapidly becoming the most significant health challenge of the 21st century. Chronic noncommunicable diseases (NCDs) are replacing infectious diseases as the most significant factor in poor global health outcomes. NCDs account for 75% of disability adjusted life years. Cancer is one of the deadliest chronic diseases and is now on the verge of overtaking heart disease as the leading cause of death in the United States. Mitochondrial dysfunction linked to nutritional imbalance, lack of physical activity, and exposure to a broad range of environmental toxins is implicated in cancer and many chronic diseases. Although nutrition and exercise recommendations have been emphasized for primary prevention, overall health remains poor due to conflicting information and the inability to easily assess adherence. The glucose ketone index (GKI) was originally developed as a quantitative point-of-care blood biomarker for assessing diet ence in cancer therapy. However, the ratio of glucose to ketones (specifically xybutyrate) can also be linked to the risk of chronic diseases and may help sk more accurately than the glucose reading alone. Low GKI ratios ed to decrease risk, while high GKI are hypothesized to compensated euglycemia may help reduce

Ketogenic Diet in Cancer Prevention and Therapy: Molecular Targets and Therapeutic Opportunities

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Cancer metabolism and dietary interventions

Lin Qian[1,2*], Fan Zhang[1,2*], Miao Yin[1,2], Qunying Lei[1,2,3,4]

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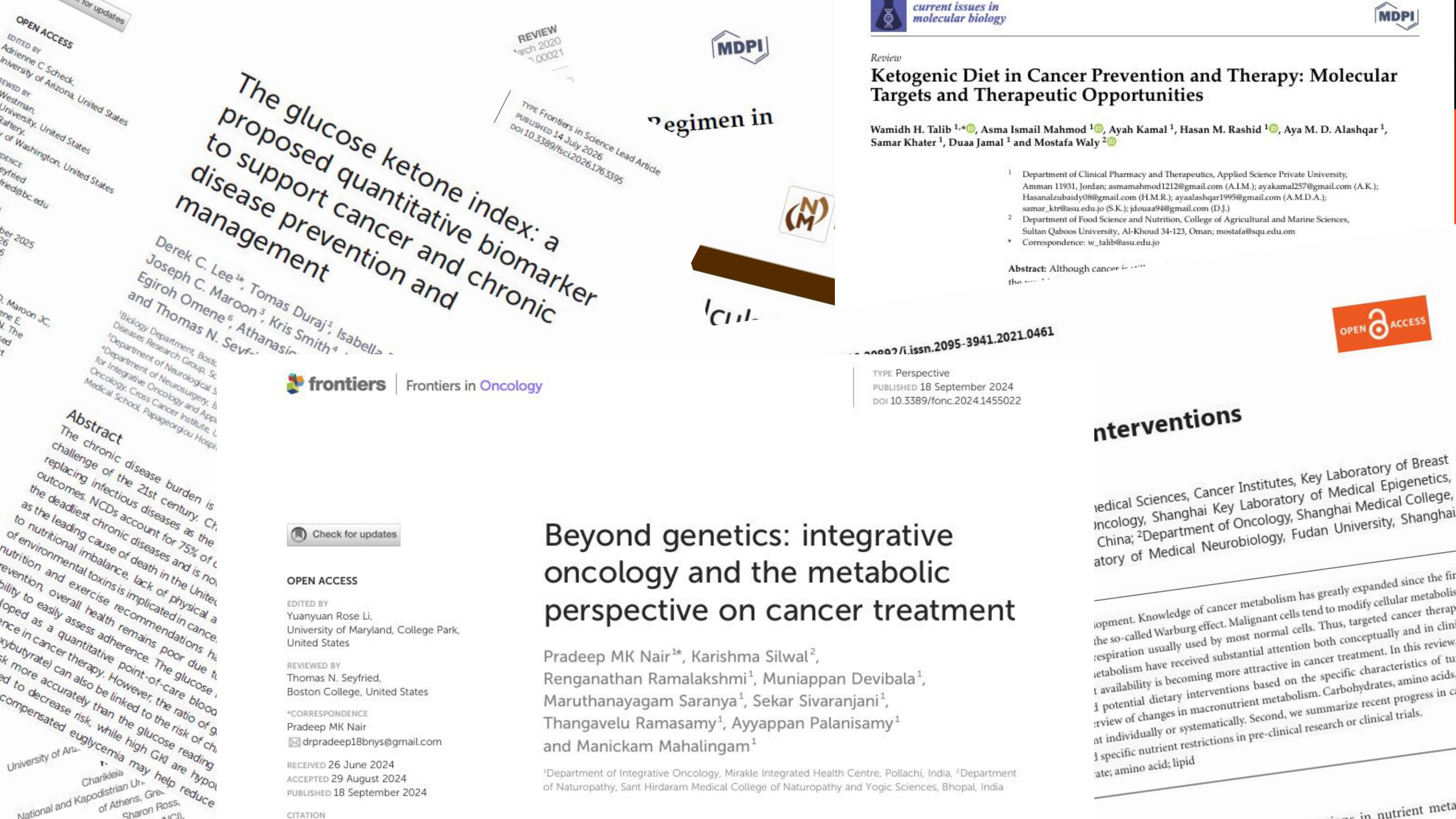
ABSTRACT

Metabolic remodeling is a key feature of cancer development. Knowledge of cancer metabolism has greatly expanded since the fir observation of abnormal metabolism in cancer cells, the so-called Warburg effect. Malignant cells tend to modify cellular metabolis to favor specialized fermentation over the aerobic respiration usually used by most normal cells. Thus, targeted cancer therap based on reprogramming nutrient or metabolite metabolism have received substantial attention both conceptually and in clini practice. In particular, the management of nutrient availability is becoming more attractive in cancer treatment. In this review, discuss recent findings on tumor metabolism and potential dietary interventions based on the specific characteristics of tu metabolism. First, we present a comprehensive overview of changes in macronutrient metabolism. Carbohydrates, amino acids, lipids, are rewired in the cancer microenvironment individually or systematically. Second, we summarize recent progress in ca interventions applying different types of diets and specific nutrient restrictions in pre-clinical research or clinical trials.

KEYWORDS

Cancer metabolism; diet intervention; carbohydrate; amino acid; lipid



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Derek C. Lee[1*], Tomas Duraj[1], Isabella
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Beyond genetics: integrative oncology and the metabolic perspective on cancer treatment

Pradeep MK Nair[1*], Karishma Silwal[2],
Renganathan Ramalakshmi[1], Muniappan Devibala[1],
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DEBATE

Clinical research framework proposal for ketogenic metabolic therapy in glioblastoma

Tomás Duraj[1*], Miriam Kalamian[2], Giulio Zuccoli[3], Joseph C. Maroon[4], Dominic P. D'Agostino[5], Adrienne C. Scheck[6], Angela Porf[5], Sebastian F. Winter[7], Jethro Hu[8], Rainer J. Klement[9], Alicia Hickson[10], Derek C. Lee[1], Isabella Cooper[11], Barbara Kofler[12], Kenneth A. Schwartz[13], Matthew C. L. Phillips[14,15], Colin E. Champ[16], Beth Zupec-Kania[17], Jocelyn Tan-Shalaby[18], Fabiano M. Serfaty[19,20], Egiroh Omene[21], Gabriel Arismendi-Morillo[22,23], Michael Kiebish[24], Richard Cheng[25], Ahmed M. El-Sakka[26], Axel Pflueger[27], Edward H. Mathews[28], Donese Worden[29], Hanping Shi[30], Raffaele Ivan Cincione[31], Jean Pierre Spinosa[32], Abdul Kadir Slocum[33], Mehmet Salih Iyikesici[34], Atsuo Yanagisawa[35], Geoffrey J. Pilkington[36], Anthony Chaffee[37], Wafaa Abdel-Hadi[38], Amr K. Elsamman[39], Pavel Klein[40], Keisuke Hagihara[41], Zsófia Clemens[42], George W. Yu[43], Athanasios E. Evangeliou[44], Janak K. Nathan[45], Kris Smith[46], David Fortin[47], Jorg Dietrich[7], Purna Mukherjee and Thomas N. Seyfried[1*]

Abstract

Glioblastoma (GBM) is the most aggressive primary brain tumor in adults, with a universally lethal prognosis despite maximal standard therapies. Here, we present a consensus treatment protocol based on the metabolic requirements of GBM cells for the two major fermentable fuels: glucose and glutamine. Glucose is a source of carbon and ATP synthesis for tumor growth through glycolysis, while glutamine provides nitrogen, carbon, and ATP synthesis through glutaminolysis. As no tumor can grow without anabolic substrates or energy, the simultaneous targeting of glycolysis and glutaminolysis is expected to reduce the proliferation of most if not all GBM cells. Ketogenic metabolic therapy (KMT) leverages diet-drug combinations that inhibit glycolysis, glutaminolysis, and growth signaling while shifting energy metabolism to therapeutic ketosis. The glucose-ketone index (GKI) is a standardized biomarker for assessing biological compliance, ideally via real-time monitoring. KMT aims to increase substrate competition and normalize the tumor microenvironment through GKI-adjusted ketogenic diets, calorie restriction, and fasting, while also targeting glycolytic and glutaminolytic flux using specific metabolic inhibitors. Non-fermentable fuels, such as ketone bodies, fatty acids, or lactate, are comparatively less efficient in supporting the long-term bioenergetic and biosynthetic demands of cancer cell proliferation. The proposed strategy may be implemented as a synergistic metabolic priming baseline in GBM as well as other tumors driven by glycolysis and glutaminolysis, regardless of their residual mitochondrial function. Suggested best practices are provided to guide future KMT research in metabolic oncology, offering a shared, evidence-driven framework for observational and interventional studies.

Keywords Cancer, Glioblastoma, Metabolism, Research design, Warburg Effect, Glutaminolysis, Precision medicine

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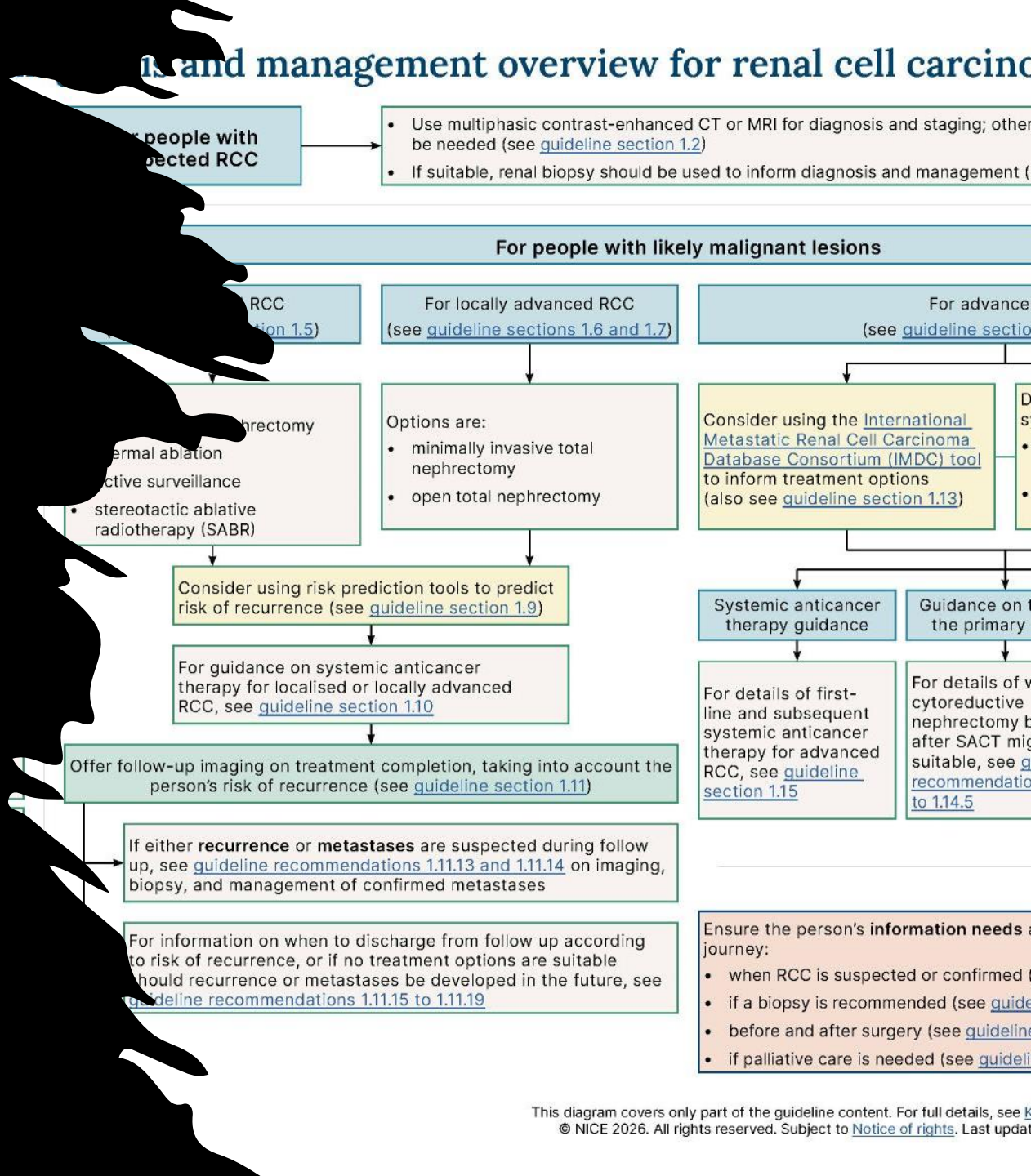
Loose Ends

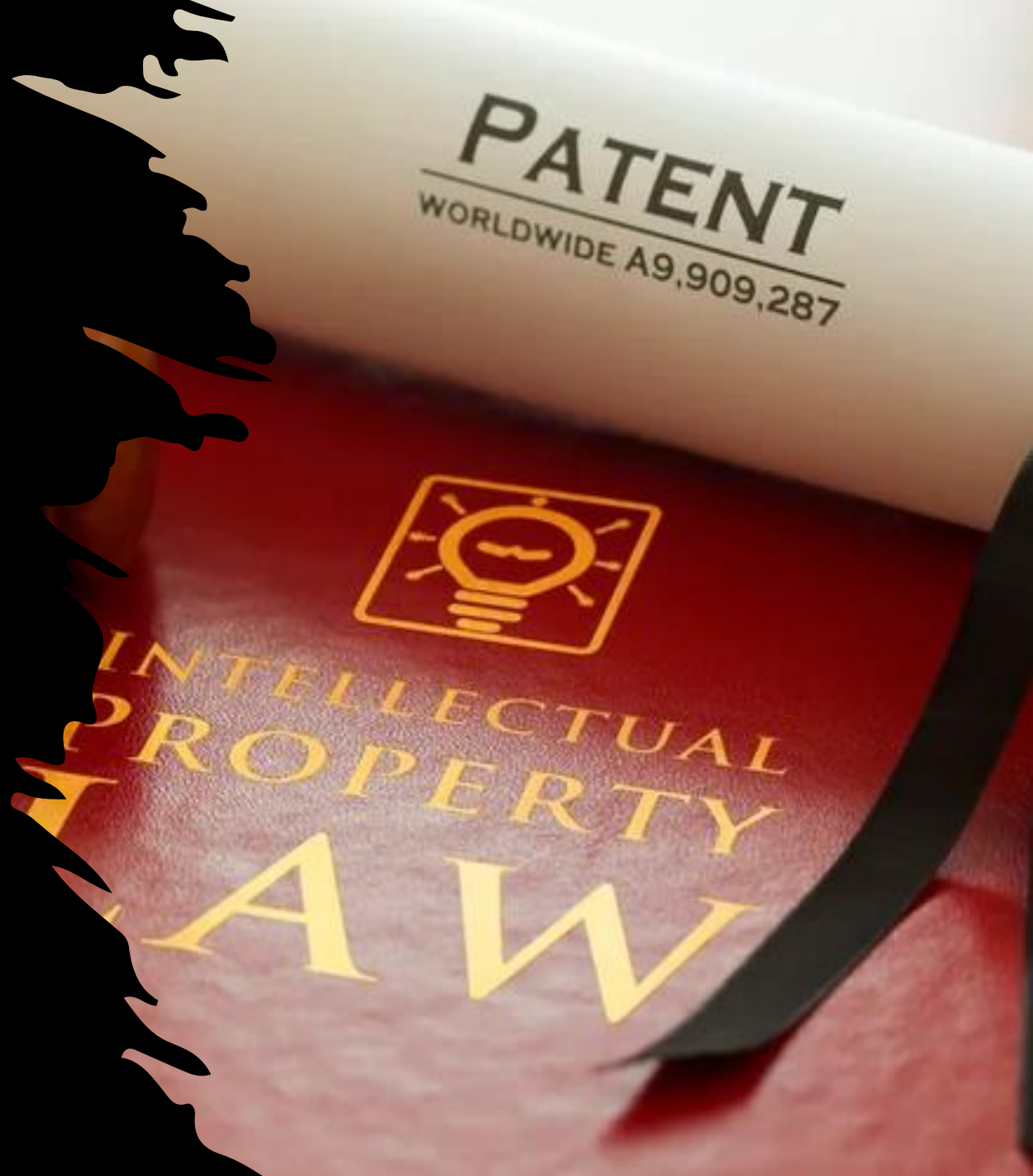
How come we don’t know about the metabolic approach?



Not in NHS and NICE guidelines



No intellectual property in nutrition or HBOT



No money in it for big pharma



No accolades for scientists



Our habits


Allergens Advice
All bread baked on site may contain traces of nuts
Brown Organic Loaf
Malted Sourdough
LARGE SOURDOUGH
£3.50

Huge reliance on grains



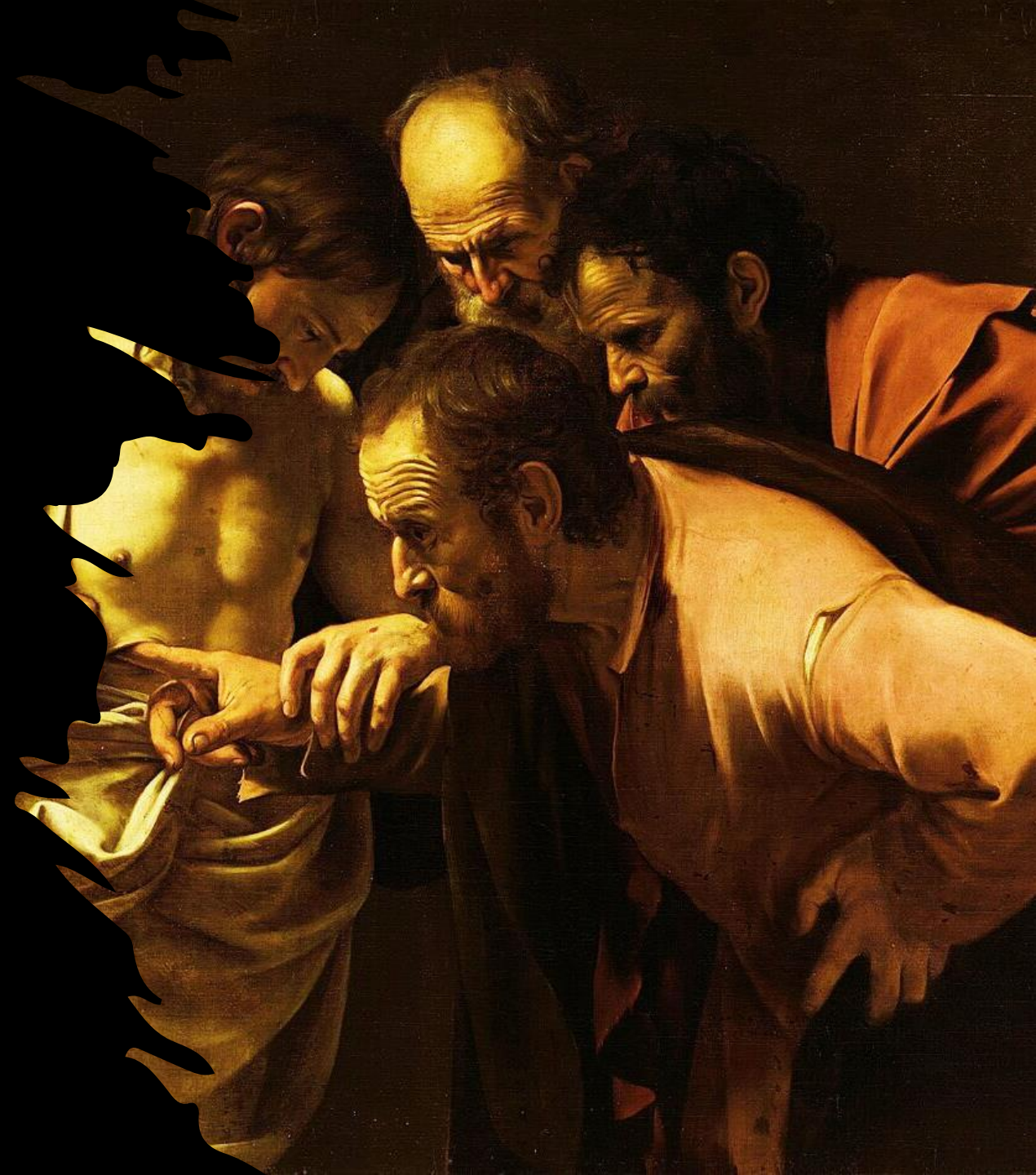
No capacity for more livestock



Medical dogma



Our natural scepticism



Okay, where’s the evidence?



There have been no studies that have passed FDA or NICE requirements. Why?

incidence of GBM is increasing in the (21).

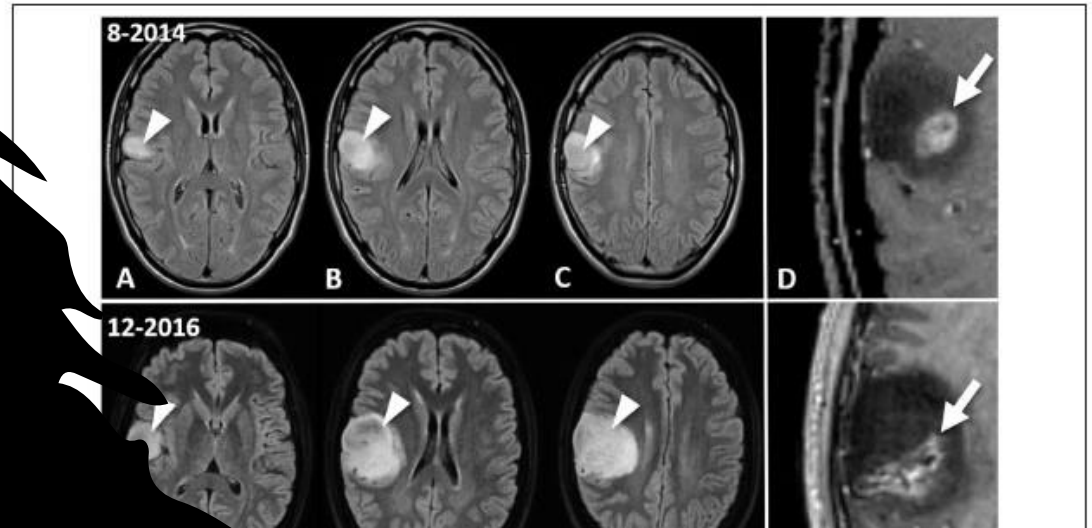
wed studies describing the adverse effects associated with the current SOC for GBM (17). GBM, like most malignant cancers, is driven by glucose and glutamine fermentation through the sis and glutaminolysis pathways, respectively (22–27). The on glucose and glutamine fermentation arises from oxidative phosphorylation (OxPhos) that is linked in the number, structure, and function of GBM tissue (17, 26–33). Surgical debulking iotherapy inadvertently increases the availability mine in the tumor microenvironment (17, apy can further damage mitochondria , increasing systemic inflammation and (36, 37). Bevacizumab is even more itochondrial dysfunction in human rkable in its ability to facilitate through the neural parenchyma and ar network (38–40). Use of dexamethasone can te GBM growth by increasing blood glucose etabolism (25, 41–44). In light of this mation, the poor progression free and overall survival rienced by most GBM patients receiving the SOC should not surprising.

drivers of rapid GBM growth while enhancing the metabolic efficiency of normal brain cells (56).

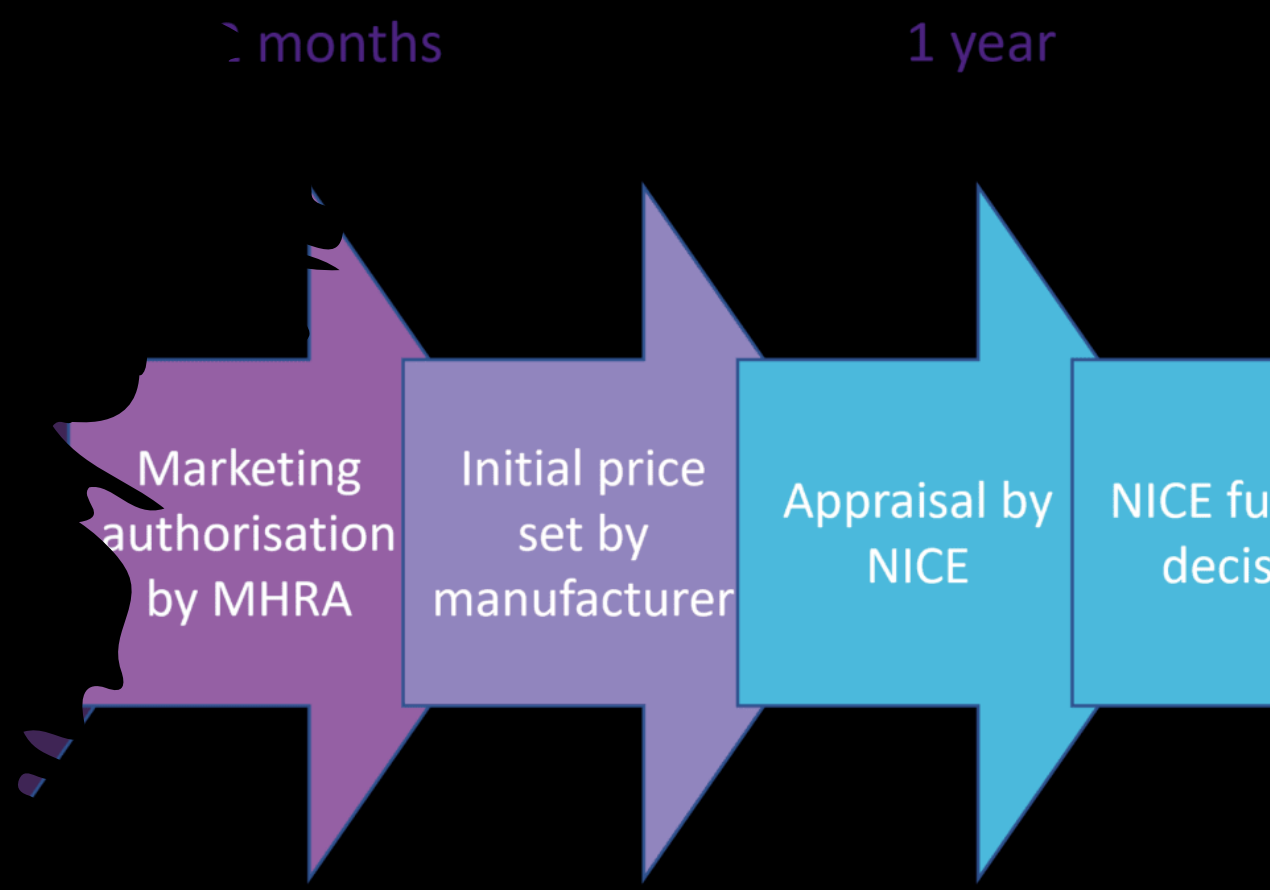
CASE REPORT

A 26-year-old male from South Devon presented on August 16, 2014 at University Hospitals Plymouth NHS Trust, PL6 8DH, UK, with two episodes of left-sided facial numbness and bilateral tonic-clonic seizures originating from the right temporal lobe. There was no history of malignancy or chronic disorders. The patient's blood pressure was within normal limits (110/70). Laboratory investigation revealed unremarkable blood chemistry, with liver and renal functions within normal limits. Fasting blood glucose and C-Reactive protein were within normal ranges. Prior to therapeutic intervention, the patient's weight, height, and body mass index (BMI) were 63 kg, 180 centimeters, and 19.4 kg/m^2, respectively. The contrast enhanced brain MRI (August 22, 2014) showed an intra-axial lesion, centered in the right inferior frontal lobe. The lesion, which was mainly non-enhancing and solid, disclosed the presence of an eccentric contrast enhancing nodule (**Figure 1, Panel 1,** D).

Enhanced MRI of the brain (August 22, 2014) showed a lobar T2 signal abnormality without restricted diffusion and with central ring enhancement centered on the opercula



Several,
Large scale,
Randomised,
Placebo-based,
Double blind,
Studies



Cost:
£100’s millions



Clearly aimed at approving drugs



Eatwell Guide

Use the Eatwell Guide to help you get a balance of healthier and more sustainable food. It shows how much of what you eat overall should come from each food group.

Check the label on packaged foods

Each serving (150g) contains

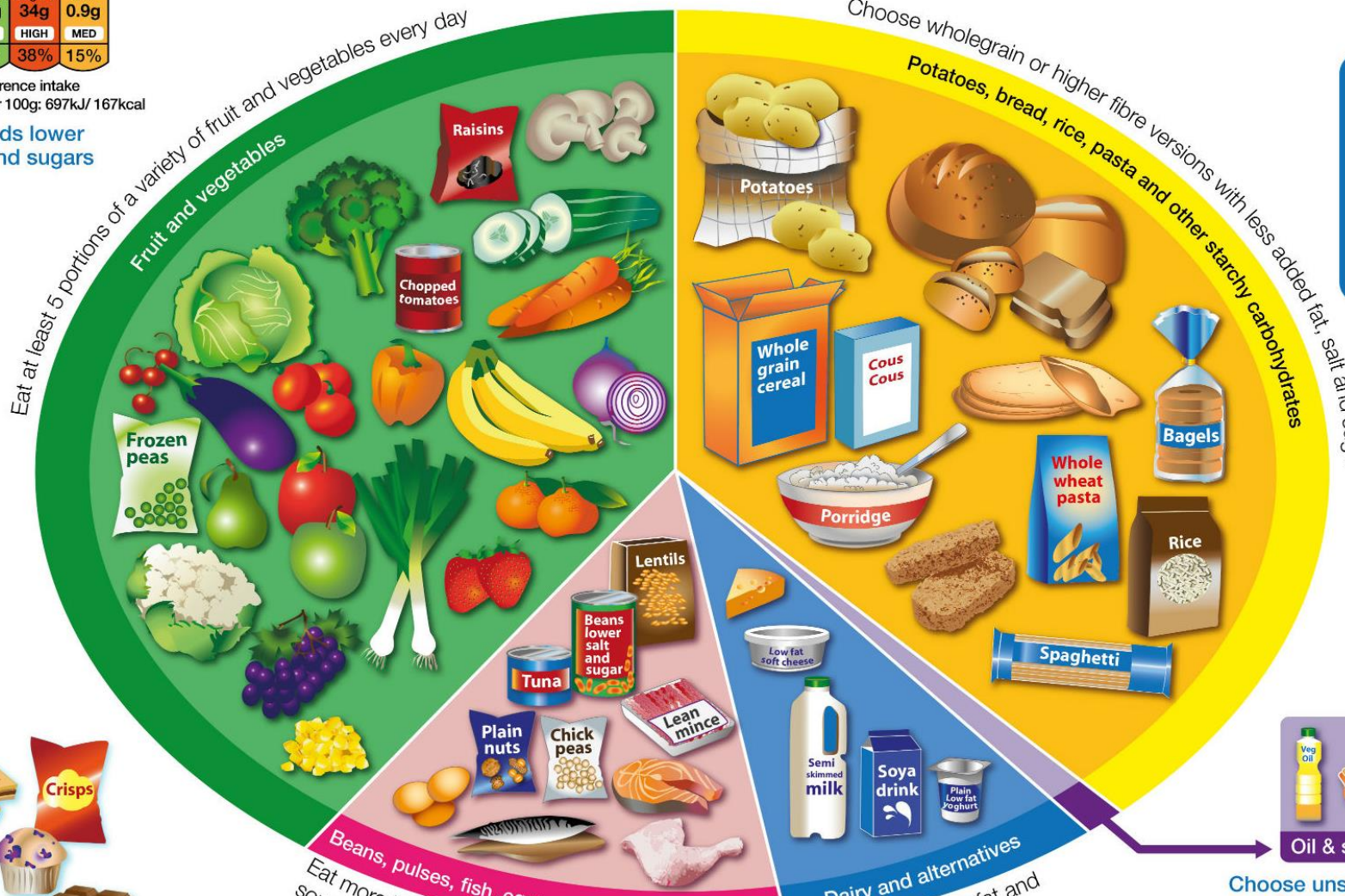
Energy	Fat	Saturates	Sugars	Salt
1046kJ 250kcal	3.0g	1.3g	34g	0.9g
	LOW	LOW	HIGH	MED
13%	4%	7%	38%	15%

of an adult's reference intake
Typical values (as sold) per 100g: 697kJ/ 167kcal

Choose foods lower in fat, salt and sugars



Eat less often and in small amounts



Eat more beans and pulses, 2 portions of sustainably sourced fish per week, one of which is oily. Eat less red and processed meat

Choose lower fat and lower sugar options

Choose unsaturated oils and use in small amounts



Water, lower fat milk, sugar-free drinks including tea and coffee all count.

Limit fruit juice and/or smoothies to a total of 150ml a day.

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

Low-Carb Diet Guide

Check the label on packaged foods

Each serving (150g) contains

Energy 1046kJ 250kcal	Fat	Saturates	Sugars	Salt
	10g HIGH	5g HIGH	2g LOW	2g HIGH
13%	70%	35%	1%	35%

Of an adult's ideal intake
Typical values (as sold) per 100g: 697 kJ/ 176 kcal

Choose foods high in fat and low in sugars and starch



Eat less often and in small amounts





Water, herbal tea, black coffee and zero-calorie drinks all count.

Eliminate all sugar drinks, fruit juices and smoothies.



Avoid all vegetable oils and fats including sunflower, rapeseed (canola), soybean, corn and palm. Use olive, avocado or coconut oil instead.

Per day 2000kcal 2500kcal = ALL FOOD + ALL DRINKS

The Metabolic Approach

Should be:

“Exceedingly usual behaviour”

The Metabolic Approach

More information, type into Google

“Metabolic Approach to Cancer Solihull”


The End

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