Integrative & Personalised Medicine 26

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Modifying Tumour Adaptation: Metabolically Targeted Adjuncts and Pragmatic Evidence in Oncology

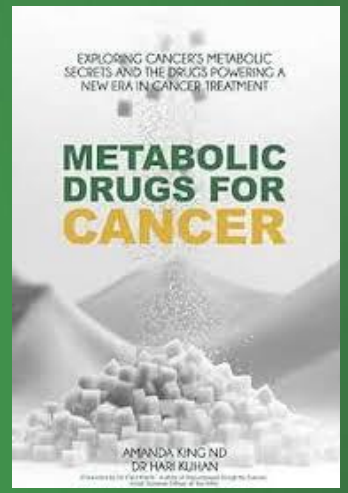
Dr Hari Kuhan

Medical Director – Lucio Health

Patient X

- Diagnosis

- Oncology Review
- Internet Searches
- Facebook Groups, Instagram
- Podcasts
- You Tube Videos
- Books



- Advise from friends, family / former patients, complete strangers !


INFORMATION

The Age of Information

A blessing and a curse

- More informed
- Better questions
- Active participation
- Not passive recipients

- Algorithms lack nuance
- Social media rewards certainty
- The loudest voice wins
- Confidence mistaken for knowledge

Nowhere is this tension more apparent than in the world of cancer.

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THE POLARIZED CONVERSATION

When Extremes Replace Nuance, Patients Lose

ONE SIDE SAYS...

- Conventional medicine is their only hope.
- Dismisses everything outside standard oncology.
- Extraordinary doses of repurposed medicines are promoted. Little discussion of safety, interactions or context.
- Certainty over complexity. Sound bites over science.
- Positions patients as followers, not partners.

VS.

THE OTHER SIDE SAYS...

- Conventional medicine is the problem.
- Presents almost every intervention as a breakthrough.
- Dismisses interesting biological signals simply because they sit outside traditional paradigms.
- Complexity is reduced to simple narratives.
- Positions patients as consumers, not individuals.

BUT WHAT CONCERNS ME MOST...

It is not that these conversations are taking place.

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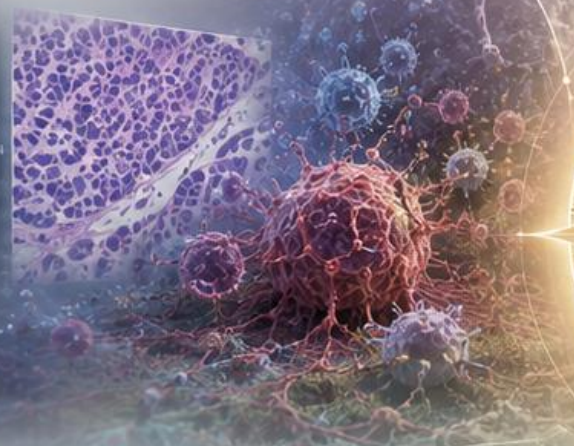
Because cancer is **nuanced.**



NUANCE

Good Medicine

Patients are **nuanced.**

Values Goals Experience Context Preferences

Biology is **nuanced.**

Genomics Pathways Biomarkers Signals Microenvironment

Certainty is often the enemy of good medicine.

My Journey to Lucio Health

- Imperial College London – MBBS
- BSc Surgery & Anaesthesia - BSc
- Medical Rotations – London – St Mary's, Chelsea & Westminster, Hammersmith
- CMT – St Bartholomew's Hospital, Colchester General
- London Oncology – Mount Vernon, UCL, Royal Marsden, St Bartholomew's
- Oncology national training number London UCL
- Barts Cancer Institute - Metabolic approaches against Pancreatic cancer stem cells
- SCRI UK – Early Phase Clinical Trials – Breast, Lung, Gynae
- Care Oncology Clinic – Medical Lead
- Lucio Health – Medical Director (CURRENT)

The Questions Patients Still Asked

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Questions conventional medicine often struggled to answer.

Questions about **nutrition**
What should I eat?

Questions about **fasting**
Should I fast?

Questions about **supplements**
What supplements are safe or helpful?

Questions about **exercise**
What kind of exercise is right for me?

Questions about **sleep**
Why is my sleep so disrupted?

Questions about **inflammation**
What fuels inflammation—and how can I reduce it?

Questions about what they themselves could do **alongside treatment**
What can I do to support my healing?

Not instead of treatment. Alongside treatment.

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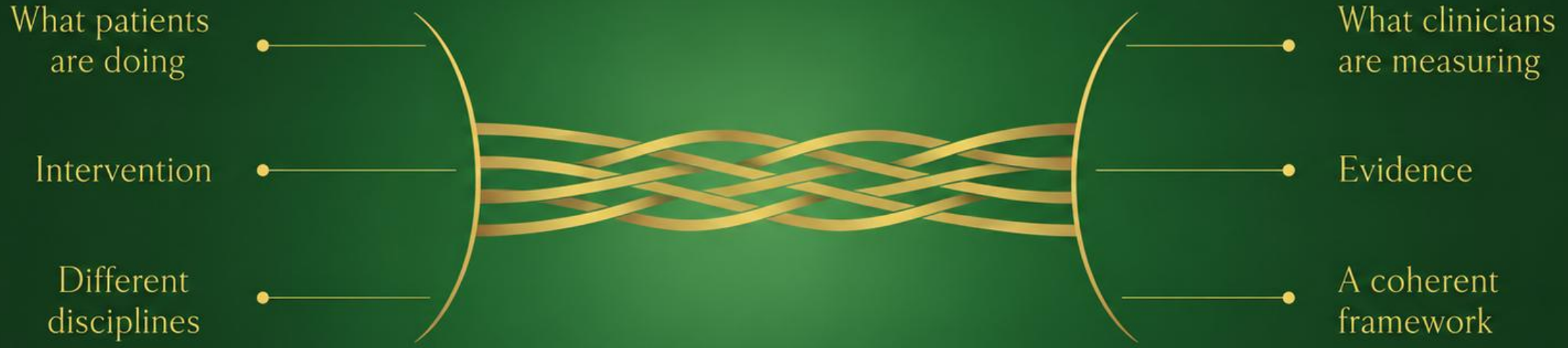
The Gap



Coexistence is not integration.

True integration means weaving different ways of thinking into a coherent whole.

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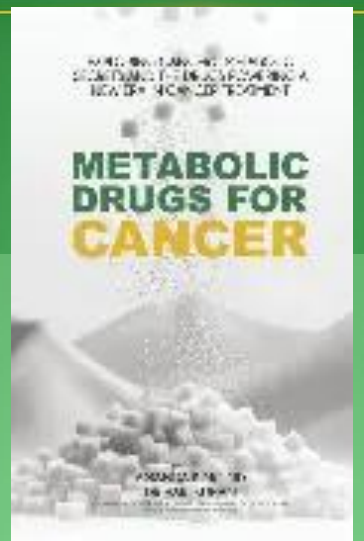
How do we improve the biological environment?

How do we support resilience?

How do we influence the conditions in which disease develops and responds to treatment?

And perhaps most importantly:

How do we do this responsibly?



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Conventional — **Test, don't guess.** — Integrative

A principle both conventional and
integrative practitioners can rally around.

Functional & Integrative Medicine Assessment

A structured systems-based view

1. Gut & Microbiome

- GI360
- GI Effects
- GI-MAP
- Stool microbiome analysis
- Digestive function
- Dysbiosis assessment

2. Hormones & Circadian Biology

- DUTCH Test
- Cortisol rhythm
- Estrogen metabolism
- Androgens
- Melatonin pathways

3. Nutritional & Metabolic Status

- NutrEval
- Micronutrient testing
- Organic acids
- Amino acids
- Fatty acids
- Oxidative stress markers

4. Environmental Exposure

- Heavy metals
- Mycotoxins
- Mould exposure
- Environmental toxins
- Chemical burden

5. Genetics & Nutrigenomics

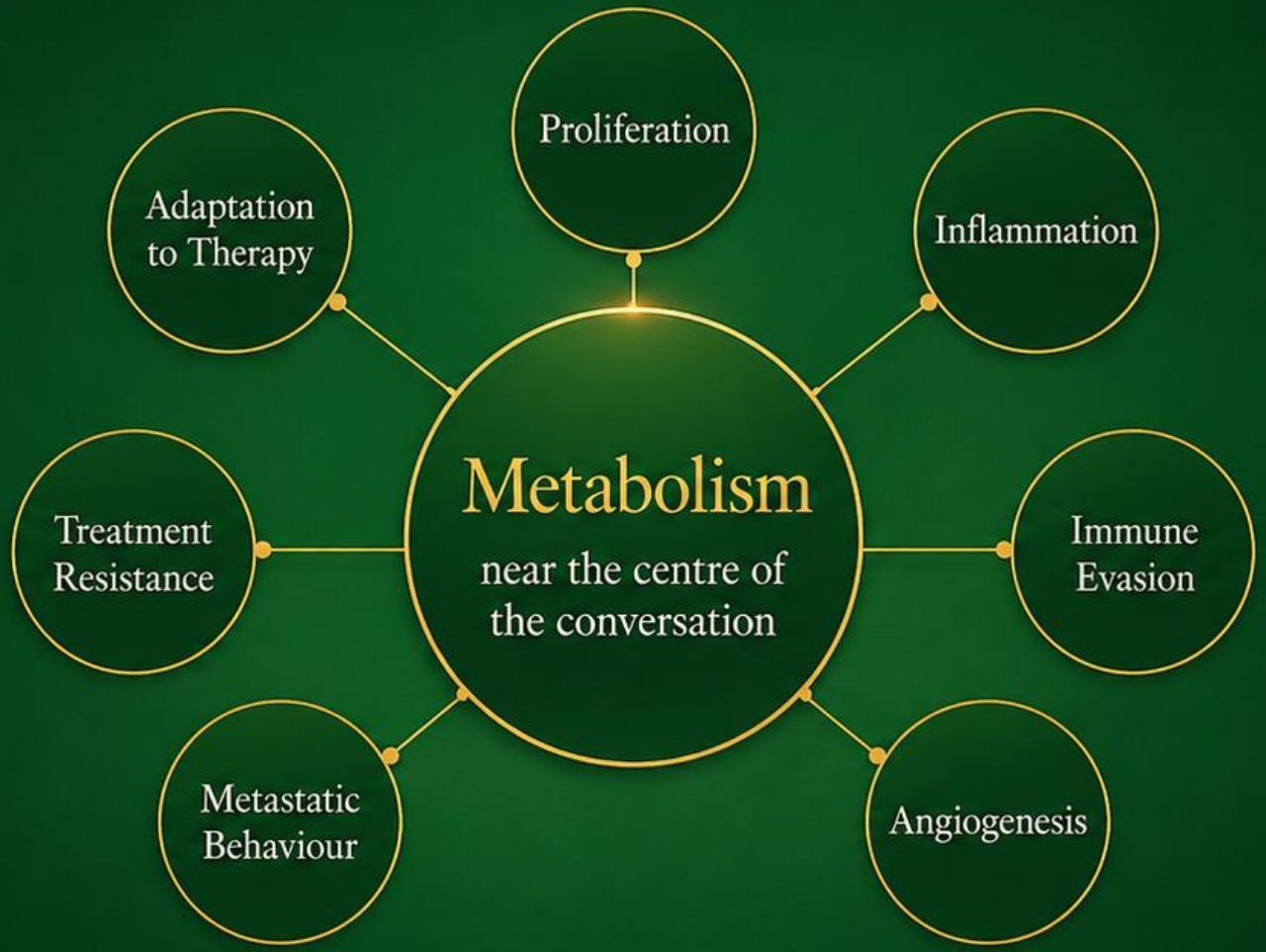
- MTHFR
- COMT
- Detoxification pathways
- Methylation profiles
- APOE

6. Chronic Infection Assessment

- EBV
- CMV
- Lyme disease
- Bartonella
- Other chronic infections

Metabolism and the Hallmarks of Cancer

Metabolism appears repeatedly across cancer biology.



Not simply glucose. Not simply mitochondria.

It is about the ecosystem in which cancer survives.

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ADAPTATION IS THE REAL ENEMY

"Cancer is not a static disease. It is an evolving ecosystem undergoing continual selection pressure."

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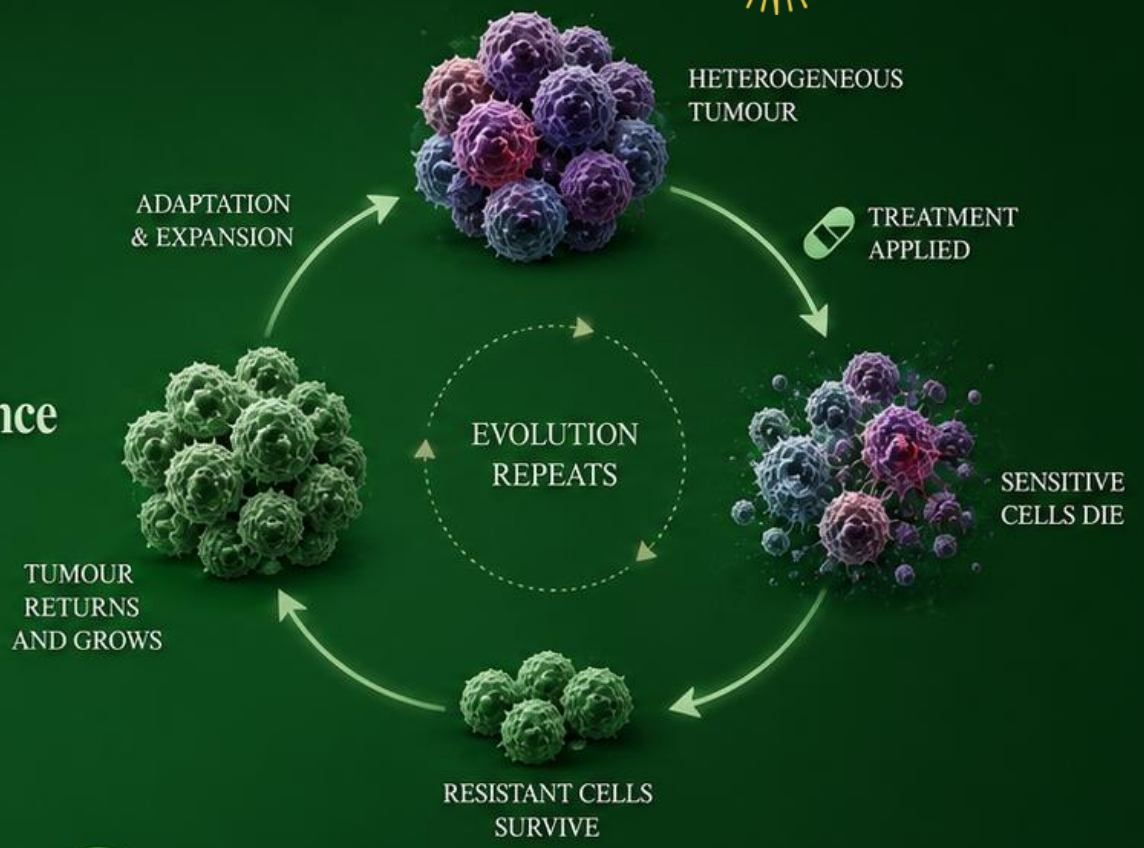
Cancer Is An Evolutionary Process

Treatment → Selection Pressure → Adaptation → Resistance

Repeat



Treatment Resistance

Almost every breakthrough in oncology eventually encounters the same problem: resistance.

Examples:

- EGFR inhibitors
- BRAF inhibitors
- Endocrine therapy
- Chemotherapy
- Immunotherapy

Initially: Tumour shrinks

Months later: Tumour returns

Not because the treatment stopped working.

Because the tumour adapted.

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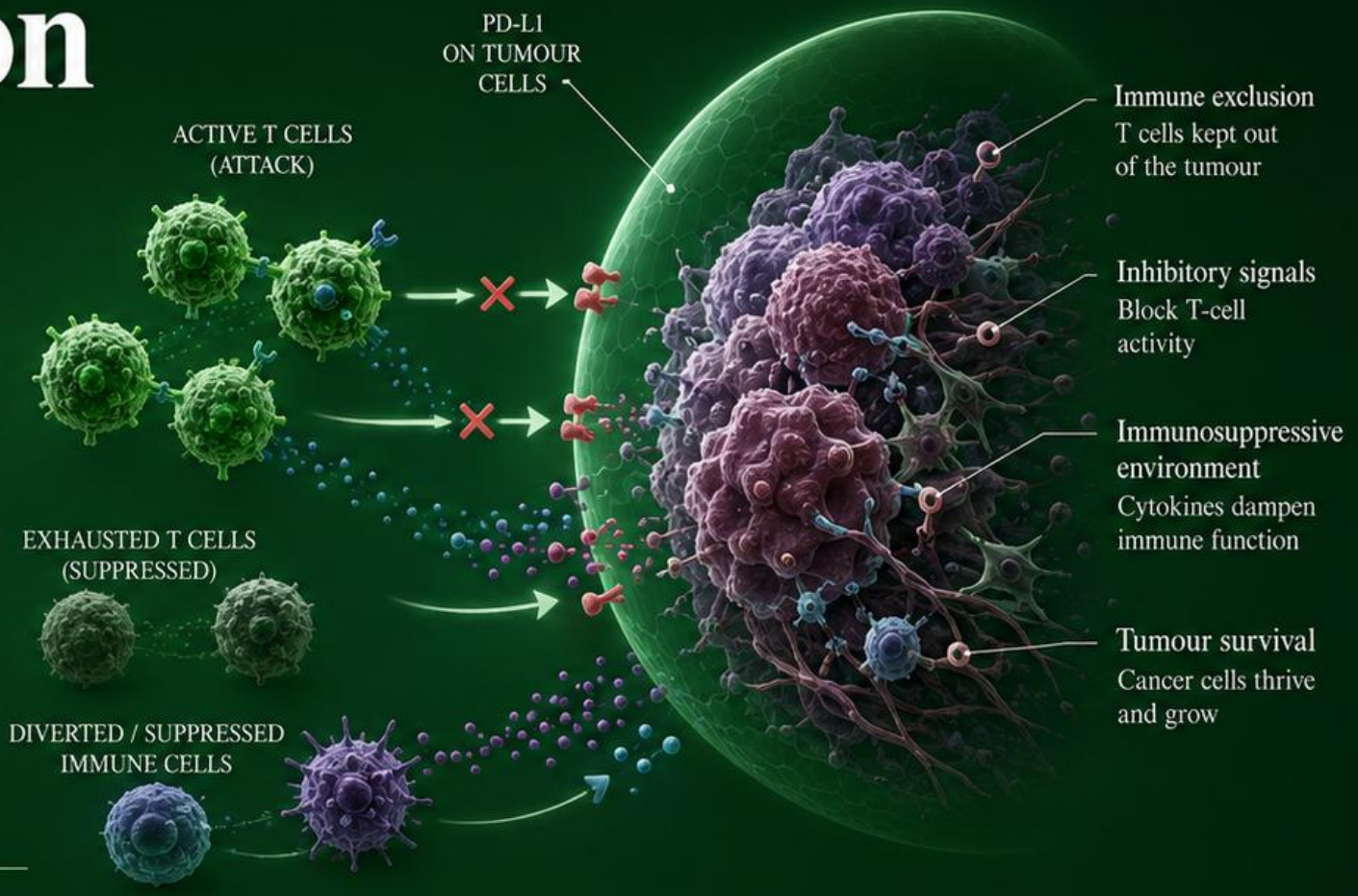
Immune Evasion

Cancer doesn't simply adapt to drugs.
It adapts to the immune system.

A healthy immune system is continually identifying and eliminating abnormal cells.

Yet established cancers survive.

Why? Because they learn to hide.



MECHANISMS OF IMMUNE EVASION

- PD-L1 expression
- T-cell exhaustion
- Immunosuppressive cytokines
- Regulatory T cells
- Myeloid suppressor cells

The tumour isn't merely avoiding destruction.
It is actively reshaping its environment
to make destruction less likely.

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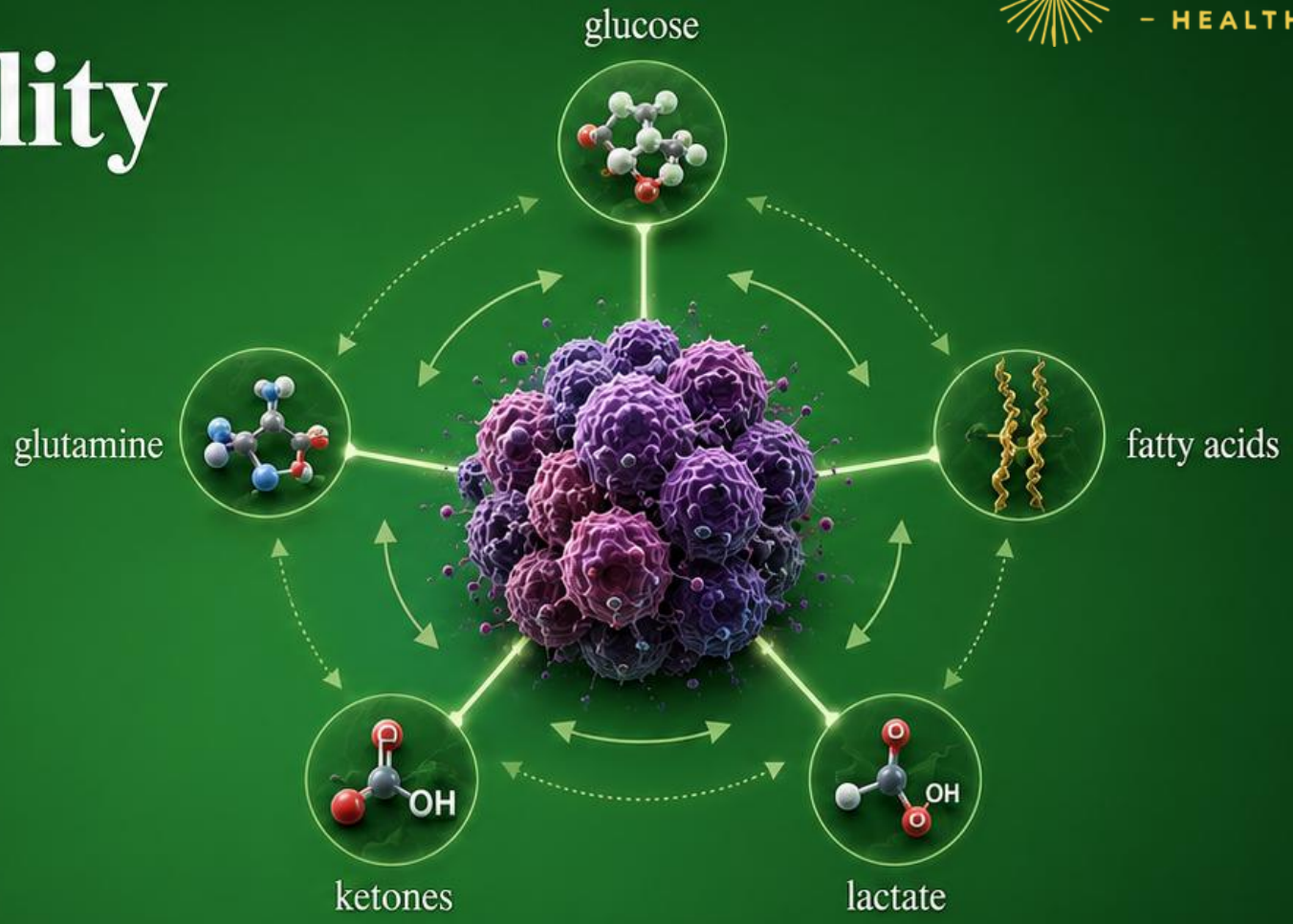
Metabolic Flexibility

A tumour doesn't rely on a single fuel source. It adapts.

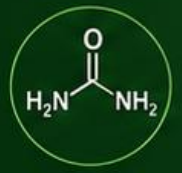
Historically:
Warburg Effect
Glucose
Aerobic glycolysis

Reality:
Much more complex.



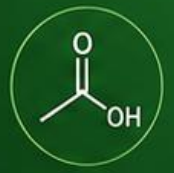
Tumours may utilise:


glucose

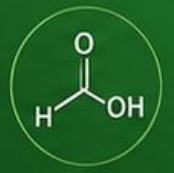


glutamine


fatty acids



ketones



lactate

depending on circumstances

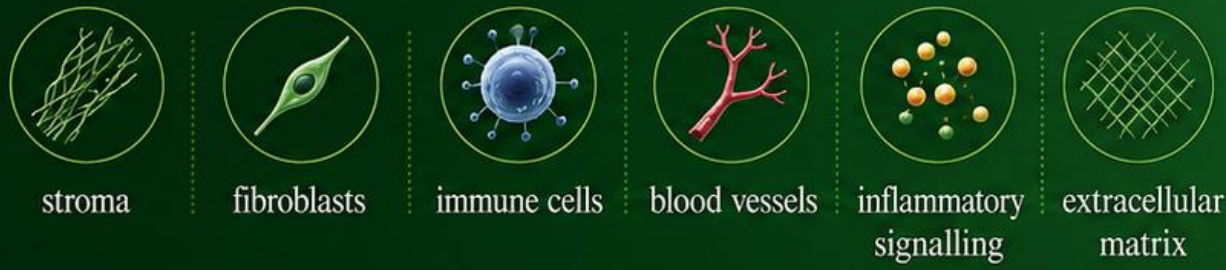
> *One of the reasons cancer is so difficult to starve is that it is metabolically opportunistic. It continually searches for alternative routes.*

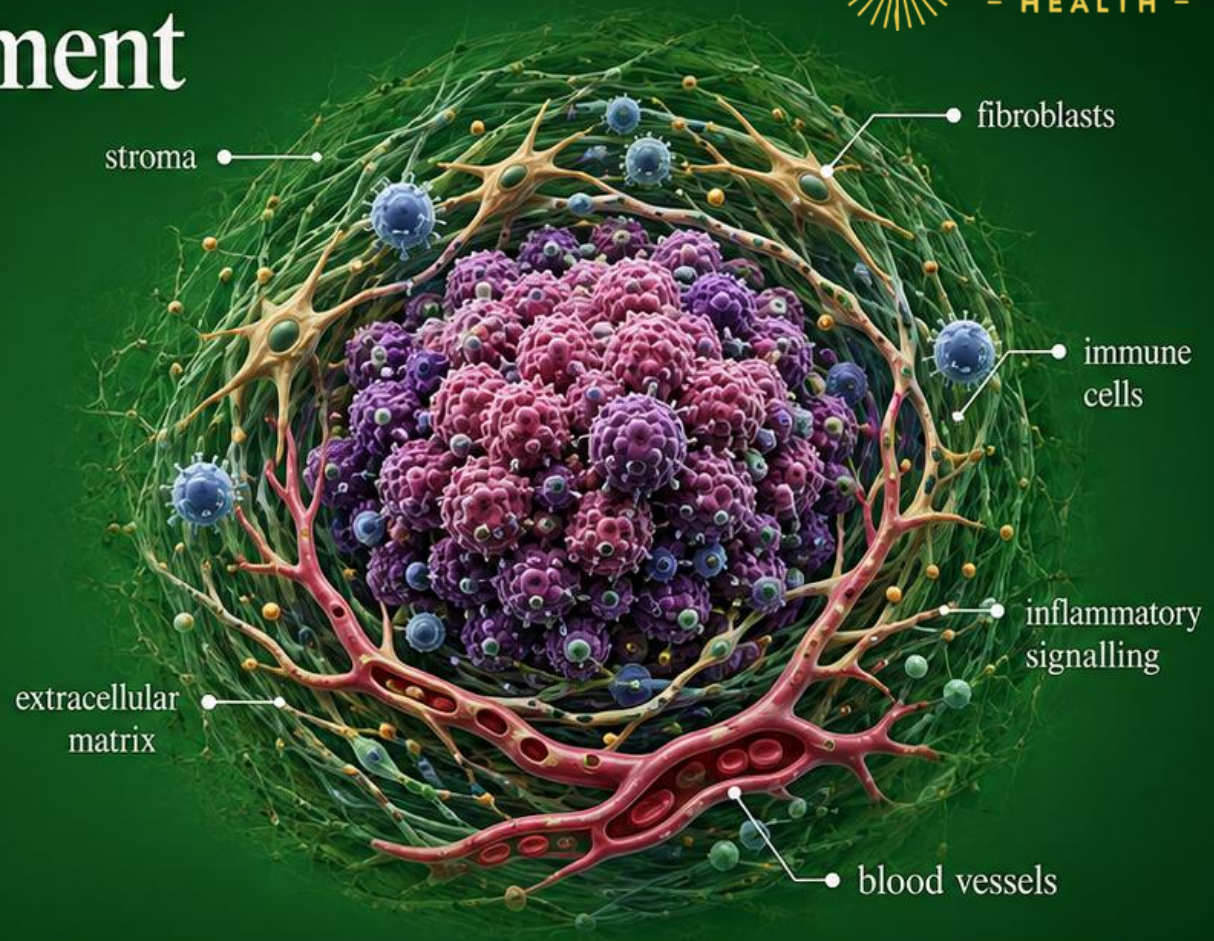
The Tumour Microenvironment

Conversations with those who work extensively in pancreatic cancer and KRAS biology have reinforced how important the surrounding environment has become in modern cancer thinking.

For years:
Focus = tumour cell

Now:
Focus increasingly includes:





Especially in pancreatic cancer.

A tumour may be surrounded by a highly protective biological fortress.

> *Increasingly, cancer is not viewed as a collection of malignant cells. It is viewed as an ecosystem.*

KRAS Inhibitor Trials

How Metabolic Oncology Can Work Alongside Conventional Chemotherapy

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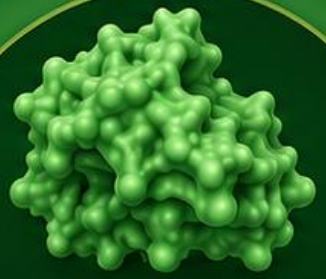
CONVENTIONAL CHEMOTHERAPY

- Targets rapidly dividing cells
- Reduces tumour burden
- Standard of care foundation
- Systemic effect



KRAS INHIBITOR TRIALS

METABOLIC ONCOLOGY SUPPORT

- Targets metabolic dependencies
- Modulates the tumour microenvironment
- Supports treatment tolerance & resilience
- Addresses adaptation & resistance pathways

POTENTIAL BENEFITS OF THE COMBINATION

- Enhance response to KRAS inhibitors and chemotherapy
- Overcome or delay resistance through metabolic targeting
- Protect normal tissues & support quality of life
- Create a less favourable ecosystem for cancer survival

TARGET THE DRIVER. RESHAPE THE ECOSYSTEM. IMPROVE OUTCOMES.

KRAS inhibitors attack the signal. Metabolic oncology transforms the soil it grows in.

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Repurposed Medications That Often Come Up

Commonly discussed in adjunctive / metabolic oncology conversations

- **Metformin**
- **Statins**
  atorvastatin, simvastatin, pitavastatin
- **Doxycycline**
- **Hydroxychloroquine**
- **Mebendazole / Fenbendazole / Niclosamide / Ivermectin**
- **Melatonin**
- **Aspirin / COX-2 pathway agents**
  aspirin, celecoxib
- **Cimetidine / antihistamine strategies**
  cimetidine, loratadine
- **Low-dose naltrexone**

• Context, safety, interactions and evidence all matter. •

Repurposed Medicines: pathways, safety and balance

Common medicines that often come up because they interact with metabolism, inflammation, autophagy, mitochondrial biology and cellular stress responses.

Medicine	Pathway themes	What makes it attractive	Key safety value
Metformin	Metabolism, insulin signalling, AMPK, cellular stress	Well-known metabolic medicine	Familiar monitoring and contraindications
Statins	Mevalonate pathway, inflammation, proliferation signals	Extensive cardiovascular safety experience	Known toxicities and interaction profile
Doxycycline	Mitochondrial biology, protein synthesis, stress responses	Licensed antibiotic with known pharmacology	Well-described dosing cautions and monitoring
Hydroxychloroquine	Autophagy, lysosomal signalling, immune modulation	Longstanding clinical use	Recognisable contraindications and surveillance
Mebendazole	Microtubules, stress adaptation, proliferation	Repurposing interest with simple oral use	Licensed medicine with known safety framework

Why this matters

- We know their toxicities
- We know their interactions
- We know their contraindications
- We know how to monitor them

This is not an argument against supplements. It is an argument for balance.

Not drugs versus supplements.

The question is: What is the right tool for this patient, at this point in time, based on this biology?

Repurposed Medicines: further examples

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Additional agents often discussed in metabolic / adjunctive oncology conversations

Medicine	Pathway themes	What makes it attractive	Key safety value
Fenbendazole / Niclosamide / Ivermectin	Microtubules, mitochondrial function, Wnt / STAT3 signalling, stress responses	Repurposing interest across several biological pathways	Existing human or veterinary familiarity, but context and dose matter greatly
Melatonin	Circadian biology, oxidative stress, mitochondrial support, immune signalling	Well tolerated, inexpensive, relevant to sleep and resilience	Long safety history and generally straightforward monitoring
Aspirin / COX-2 pathway agents *aspirin, celecoxib*	Inflammation, prostaglandins, platelet signalling, tumour microenvironment	Clear anti-inflammatory rationale and broad biological relevance	Well understood toxicities, contraindications and monitoring
Cimetidine / antihistamine strategies *cimetidine, loratadine*	Histamine signalling, immune modulation, inflammation, microenvironment	Interesting low-cost immunologic and inflammatory signals	Licensed medicines with familiar interaction profiles
Low-dose naltrexone	Immune modulation, endorphin signalling, inflammation, stress responses	Growing interest in resilience, symptoms and immune balance	Generally well tolerated with recognisable contraindications

Why this matters

- We know their toxicities
- We know their interactions
- We know their contraindications
- We know how to monitor them

Not drugs versus supplements.

The question is: What is the right tool for this patient, at this point in time, based on this biology?

The Lucio Health Paradigm

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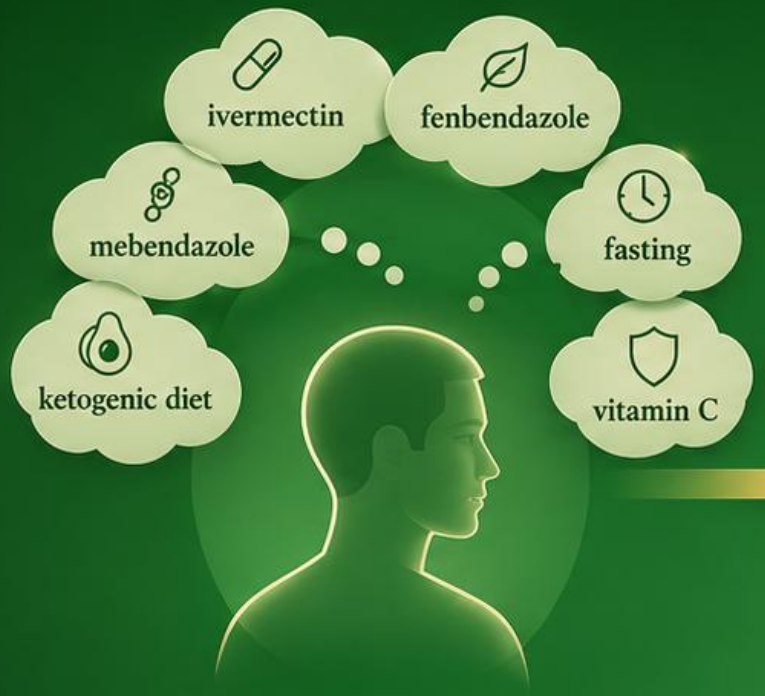
We do not begin by asking what to add. We begin by understanding.



Patients often arrive after weeks of online research

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Structured, patient-centred assessment

We begin by understanding

1. Diagnosis
2. Pathology
3. Staging
4. Conventional treatment plan
5. Blood results
6. Current medications
7. Physiological reserve
8. Goals
9. Fears

Before deciding what a patient should take, we first understand the biology, the treatment context and the person in front of us.

Precision medicine begins with characterisation.

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Next-generation sequencing, ctDNA and functional profiling help inform strategy.

1. Characterisation

- Next-generation sequencing
- ctDNA review
- Functional platforms in selected cases

FOUNDATION ONE · GUARDANT360 · ONCOLOGICA · CARIS · DATAR EXACTA · CHEMOSCALE

2. Biological insight

Personalised medicine without characterisation is simply personalised guessing

3. Strategy

- Biology
- Context
- Treatment plan
- Patient factors
- Strategy

Only then do we begin to formulate a strategy.

Not a protocol.

A strategy.

CASE STUDY 1

Metastatic Pancreatic Adenocarcinoma

"The KRAS Patient"

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Clinical presentation

A 62-year-old gentleman presents with metastatic pancreatic adenocarcinoma involving the pancreas, liver and regional lymph nodes.

Pancreas

Liver

Lymph Nodes

Following diagnosis, he commences first-line modified FOLFIRINOX. Comprehensive molecular profiling is performed.

Chemotherapy (FOLFIRINOX)

FoundationOne Findings

- KRAS G12D
- TP53 mutation
- CDKN2A loss
- SMAD4 mutation
- MSS
- Low tumour mutational burden

Biological Themes

- KRAS-driven signalling
- Tumour suppressor disruption
- Limited likelihood of benefit from checkpoint inhibitor monotherapy
- Aggressive metabolic adaptation
- Stromal protection
- Immune suppression
- Treatment resistance

Datar Exacta findings

The report demonstrates:

- Predicted sensitivity to FOLFIRINOX components
- Evidence supporting fluoropyrimidine activity
- Signal for benefit from statin exposure
- Signal for metformin sensitivity
- Potential synergy with doxycycline-mediated mitochondrial targeting
- Increased inflammatory signalling pathways
- Elevated markers associated with EMT and metastatic competence

Not a protocol. A strategy.

This is a genomically complex pancreatic cancer in which molecular profiling and functional testing help move from broad treatment categories toward a biology-informed strategy.

KRAS signalling • metabolism • inflammation • EMT • treatment resistance

FOUNDATIONONE FINDINGS

INTERPRETATION: SCIENCE AND WHAT IT MEANS

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FINDING	SCIENTIFIC EXPLANATION (THE BIOLOGY)	LAYMAN TERMS (WHAT IT MEANS)
KRAS G12D	Activating point mutation in the KRAS gene leading to constitutive (on-going) activation of KRAS signalling pathways, particularly MAPK and PI3K–AKT, promoting cell proliferation, survival, metabolic rewiring and therapy resistance.	This is a key "driver" mutation. It keeps the cancer growth engine switched on, helping the tumour grow, survive and resist many treatments.
TP53 mutation	Loss-of-function mutation in TP53, a critical tumour suppressor gene that regulates DNA damage response, apoptosis and cell-cycle arrest.	The cell's "quality control" system is broken. Damaged cells are less likely to self-destruct, allowing the cancer to survive and become more aggressive.
CDKN2A loss	Deletion or inactivation of CDKN2A (commonly p16INK4a), which normally inhibits CDK4/6 and controls the G1–S transition in the cell cycle.	The brakes on cell division are removed. Cells can divide more freely, which helps the cancer grow faster.
SMAD4 mutation	Inactivating mutation in SMAD4, a central mediator of TGF-β signalling, which regulates cell growth, differentiation, apoptosis and interaction with the tumour microenvironment.	The cancer loses an important control pathway that normally keeps growth in check and maintains normal tissue behaviour. This is linked to invasion and spread.
MSS (Microsatellite Stable)	No evidence of microsatellite instability. The DNA mismatch repair system is intact.	This tumour does not have the type of DNA error pattern that tends to respond well to immunotherapy.
Low Tumour Mutational Burden (TMB)	The tumour has a relatively low number of non-synonymous somatic mutations across its genome.	There are fewer "flags" on the cancer cells for the immune system to see. This means immunotherapy alone is less likely to be effective.

Case Strategy: Diet, Supplements and Repurposed Medicines

Supporting the biology surrounding the tumour while conventional therapy remains central

Dietary Strategy

- Moderate carbohydrate-controlled Mediterranean-style approach
- Goal is not extreme ketosis
- Focus on metabolic flexibility
- Glycaemic stability
- Preservation of lean body mass
- Attention to pancreatic exocrine insufficiency
- Protein intake and weight maintenance

Supplement Strategy

- Vitamin D3/K2
- Omega-3 fatty acids
- Curcumin
- Sulforaphane
- Medicinal mushrooms
- Magnesium
- Protein optimisation

Repurposed Medicines

- Metformin
- Atorvastatin
- Doxycycline
- Melatonin

The rationale is not that any one of these drugs targets *KRAS* directly.

The strategy is to support metabolism, inflammation, resilience and the broader biological environment around the tumour.

Why these agents may matter

Not because they target KRAS directly, but because they may influence the biology around the tumour

The rationale is not that any one of these drugs targets KRAS directly.

The conventional oncology plan remains central.

Adjunctive rationale

1. Cellular energetics
2. Mitochondrial adaptation
3. Inflammatory signalling
4. Stress response pathways

The objective is not replacement of oncology.

The objective is modification of the biological environment.

Precision Oncology in KRAS-Mutant Pancreatic Cancer

Current trial agents and how an integrated strategy may fit around them

1. Characterise the biology

- Next-generation sequencing
- ctDNA where available
- KRAS subtype matters
- Co-mutations and resistance biology
- Performance status and treatment context

Precision oncology begins with characterisation.

2. Current KRAS / RAS-targeted trial examples

Daraxonrasib (RMC-6236)	pan-RAS(ON) inhibitor	phase 3 in pancreatic cancer
Zoldonrasib (RMC-9805)	KRAS G12D-selective inhibitor	clinical development
KST-6051	pan-KRAS inhibitor	early-phase clinical development

- *Examples shown are selected current trial agents, not an exhaustive list.*

3. How might we integrate this?

Patient-specific strategy

- KRAS inhibitor if eligible / available
- Chemotherapy if required
- Radiotherapy where indicated
- Nutrition and metabolic support
- Supplements / integrative therapies
- Monitoring of safety, interactions and tolerance

The aim is not either/or.

It is precision oncology + supportive metabolic and integrative care, organised around the biology, the treatment plan and the patient.

CASE STUDY 2

Metastatic ER Positive Breast Cancer

The Endocrine Resistance Patient

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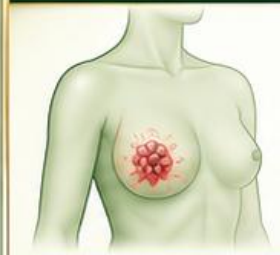
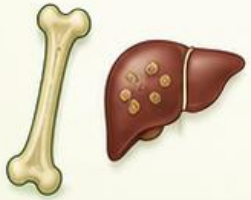
Clinical presentation



A 54-year-old woman presents with metastatic ER-positive HER2-negative breast cancer involving bone and liver.



She initially responded well to endocrine therapy but subsequently develops progression.

Comprehensive genomic profiling is undertaken.

FoundationOne findings

- ESR1 mutation
- PIK3CA mutation
- FGFR1 amplification
- CCND1 amplification
- Low tumour mutational burden
- MSS

Biological themes

Endocrine resistance	Oestrogen-independent signalling	PI3K-AKT-mTOR activation
Persistent growth signalling	Proliferative drive	Limited immunotherapy signal

This is a tumour characterised by endocrine resistance and persistent activation of growth signalling pathways. The biology suggests ongoing oestrogen-independent signalling alongside activation of the PI3K-AKT-mTOR axis.

DATAR Exacta findings

The report demonstrates:

- Predicted sensitivity to endocrine therapy combinations
- PI3K — Signal for PI3K pathway targeting
- Sensitivity signal supporting statin exposure
- Potential sensitivity to metformin-mediated metabolic modulation
- Increased inflammatory signalling activity
- Evidence of persistent proliferative signalling despite endocrine therapy

Conventional treatment remains central

- Fulvestrant
- G1 S — CDK4/6 inhibition

The adjunctive programme is then constructed.

Not 'Which supplement should we use?'

What biological vulnerabilities can we identify?

Case Study 2: FoundationOne Findings Explained

Scientific explanation and layman's interpretation

Finding	Scientific explanation	Layman terms
ESR1 mutation	Mutation in the oestrogen receptor gene, often affecting the ligand-binding domain, allowing oestrogen receptor signalling to remain active despite endocrine therapy, particularly aromatase inhibition.	The breast cancer has found a way to keep using hormone signals even when hormone treatment is trying to block them.
PIK3CA mutation	Activating mutation in the PI3K pathway, driving AKT-mTOR signalling, cell survival, growth and metabolic adaptation.	A major growth and survival pathway is switched on, helping the cancer keep growing and adapting.
FGFR1 amplification	Increased copies of the FGFR1 gene enhance receptor tyrosine kinase signalling, promoting proliferation and contributing to endocrine resistance.	The cancer has extra copies of a growth-signalling gene, which may help it resist hormone therapy and continue growing.
CCND1 amplification	Amplification of CCND1 increases cyclin D1 activity, accelerating CDK4/6-mediated G1-S cell-cycle progression and cellular proliferation.	The cancer has a stronger signal telling cells to divide, so it can multiply more quickly.
Low tumour mutational burden	A relatively low number of mutations suggests fewer neoantigens and often a less immunogenic tumour microenvironment.	There are fewer abnormal flags for the immune system to recognise, so immunotherapy on its own may be less helpful.
MSS	Microsatellite stable disease indicates intact mismatch-repair function without microsatellite instability.	This cancer does not have the DNA repair pattern that sometimes makes immunotherapy work better.

Overall picture: an **endocrine-resistant, biologically active** ER-positive breast cancer with persistent growth signalling and **limited likelihood of benefit** from checkpoint inhibitor monotherapy.

Case Strategy: Nutrition, Supplements and Repurposed Medicines

Supporting metabolic health while conventional oncology remains central

Nutrition Strategy

- Focus is placed on:
  - insulin regulation
  - body composition
  - reduction of visceral adiposity
  - Mediterranean dietary principles
- The objective is not weight loss per se.
- The objective is improvement of metabolic health.

Supplement Strategy

- Vitamin D3/K2
- Omega-3 fatty acids
- Curcumin
- EGCG
- Sulforaphane
- Magnesium

Repurposed Medicines

- Metformin
- Atorvastatin
- Melatonin

Additional therapies are introduced gradually according to tolerance and evolving clinical circumstances.

Again, the rationale is not direct tumour killing.

The rationale is influence over:

- insulin signalling
- inflammatory pathways
- cellular energetics
- adaptive stress responses

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The Intervention Is Not The Drug

Pancreatic Cancer Patient

- Different genetics
- Different microenvironment
- Different conventional treatment
- Different goals
- Different adjunctive plan

VS.

ER+ Breast Cancer Patient

- Different genetics
- Different hallmarks
- Different resistance mechanisms
- Different conventional treatment
- Different adjunctive plan

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Monitoring, Review and the Evidence Problem

Regular review is essential — but this is also where the evidence problem begins.

Ongoing review

- The patient is reviewed regularly.
- Bloods are monitored.
- Liver function is monitored.
- Tumour markers are monitored.
- Imaging is reviewed.
- Tolerance is assessed.
- The plan evolves over time.

Where the evidence problem begins

- Real patients change over time.
- Multiple variables are moving at once.
- Attribution becomes difficult.

Good clinical care is iterative.

But once multiple interventions, timing changes and evolving biology interact, certainty becomes much harder.

Where the evidence problem begins

- And this is precisely where the evidence problem begins.
- Which component contributed most?
- The chemotherapy?
- The statin?
- The metformin?
- The dietary intervention?
- The honest answer is that we do not know.

⇒ The intervention is not a drug.

⇒ The intervention is a system.

The central problem

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Evidence generation

Traditional research

Designed to study individual interventions

- One drug
- One target
- One endpoint
- One answer

Personalised integrative oncology

- Does not operate that way
- Patients receive systems
- Not variables

The intervention is not metformin.
It is not a statin.
It is not a supplement.
The intervention is the entire system.
And systems are difficult to study.

Evaluating Data Critically

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1. As physicians, one of the most important skills we develop is not simply acquiring knowledge.
2. It is learning how to critically evaluate data.
3. Learning how to resist premature conclusions.
4. Learning how to distinguish signal from noise.

Why this matters

- Data is not neutral.
- Data can be overhyped.
- Data can be underappreciated.
- Data can be selectively interpreted.
- In the wrong hands, data can be manipulated to support almost any narrative.

The danger

- One individual sees a breakthrough. Another sees nothing.
- One person overstates a signal. Another dismisses it entirely.
- Both may be wrong.
- Interpretation increasingly follows ideology rather than curiosity.

The challenge is remaining intellectually honest — particularly when dealing with imperfect information.

Perhaps the greatest professional hazard in medicine is becoming attached to a narrative.
Because once we become attached to a narrative, we stop learning.

Building Systems That Learn

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The future of Lucio Health as a learning healthcare platform

This is why I have become increasingly interested in building systems that learn.

For several years I have been asking myself a simple question:

What would happen if every patient journey could be captured in a structured and meaningful way?

Not simply the diagnosis. But:

- biology
- interventions
- timelines
- outcomes
- successes
- failures

What if we could…

collect that information prospectively → organise it → analyse it → learn from it

This is where I believe the future of Lucio Health lies.
Not simply as a clinic.
But as a **learning healthcare platform**.
One capable of transforming individual patient journeys into structured knowledge.

"Transforming individual patient journeys into structured knowledge."

Artificial Intelligence and Ethically Governed Learning

Using AI to help clinicians learn — not to replace clinical judgement

This is also where artificial intelligence becomes genuinely interesting.

What AI should not be

- Not as a replacement for clinicians
- Not as an automated treatment engine

What AI can be

- A memory system
- A pattern recognition tool
- A way of identifying trends across thousands of data points that would otherwise remain invisible

The real ambition

- The ambition is not to teach machines how to treat patients.
- The ambition is to help clinicians learn from patients more effectively.

Built responsibly

- Data must remain secure
- Consent must be explicit
- Governance must be robust
- Patients must remain partners rather than subjects

The objective is not algorithmic medicine.
The objective is ethically governed learning.

Bridging Disciplines

The future of metabolically targeted interventions

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Ultimately, I have come to believe that the future of metabolically targeted interventions will not be determined by any single repurposed medicine.

- Nor by any single supplement.
- Nor by any single protocol.
- Nor by any single medicine.

It will be determined by our ability to bridge disciplines.

Precision oncology	To combine *precision oncology* with *physiological medicine*.	Physiological medicine
Conventional science	To combine *conventional science* with *integrative thinking*.	Integrative thinking
Personalised care	To *personalise care* without abandoning *rigour*.	Rigour
Complexity	To embrace *complexity* without abandoning *evidence*.	Evidence

The future is not a single intervention. It is the disciplined integration of many ways of knowing.

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The challenge facing personalised integrative oncology

> The challenge facing personalised integrative oncology is **not deciding what to do.**
>
> The challenge is **learning from what we have done** when ***every patient's intervention is different.***

How Do We Validate Personalised Metabolic Oncology?

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1. Multiple interventions
2. Different patients
3. Different tumours
4. Different conventional treatments
5. Evolving plans
6. Multiple endpoints

"Traditional RCTs were designed for simple interventions. We are attempting to study complex adaptive systems."

OPTION 1

Become More Reductionist

"The Classical Trial Approach"

This is the most conventional solution.

Pick:

- one tumour type
- one stage
- one line of therapy
- one age range
- one protocol

For example:

- Stage IV KRAS-mutated pancreatic cancer
- Receiving FOLFIRINOX
- Age 50–75
- Metformin + Atorvastatin added
- Then compare against control

Advantages

- familiar methodology
- high credibility
- regulatory acceptance
- statistically robust

Disadvantages

- expensive
- slow
- may take years
- excludes many patients
- doesn't reflect real-world integrative practice

> *"The more scientifically clean we make the study, the less representative it becomes of actual integrative oncology."*

OPTION 2

The Learning Healthcare System

"Every Patient Becomes A Data Point"

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This is where Lucio Health comes in.

Rather than forcing every patient into one protocol:

Capture:

- tumour biology
- genomics
- DATAR
- bloods
- medications
- supplements
- outcomes

Prospectively.
Systematically.
Repeatedly.

Continuous clinical learning

Data in
↓
Patterns identified
↓
Practice adapts
↓
Outcomes improve

Advantages

- reflects real-world practice
- scalable
- captures complexity
- captures failures
- captures adaptation

Weaknesses

- observational
- confounding
- selection bias
- requires sophisticated analysis

> *"The challenge is not collecting the data. The challenge is learning from it."*

OPTION 3

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AI-Augmented Pattern Recognition

The most futuristic section — without overselling it

The audience will love it. The key is not to oversell.

What AI Is Bad At

- deciding treatment
- understanding context
- replacing clinicians

What AI Is Good At

- remembering
- organising
- pattern recognition
- detecting weak signals

Imagine: 10,000 patient journeys

Each with:

- diagnosis
- mutations
- ctDNA
- DATAR
- treatment exposures
- supplements
- repurposed drugs
- outcomes

No human can process that.

AI potentially can.

AI helps detect patterns across complexity — it does not replace clinical judgement.

> *"The ambition is not to teach machines how to treat cancer.*
> *The ambition is to help clinicians learn from complexity."*

OPTION 4

Functional Precision Oncology

Linking biological behaviour to individualised care

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This one is very important because it links directly to DATAR.

Traditional oncology asks:

What Does The Tumour Look Like?

- KRAS
- ESR1
- PIK3CA
- TP53

Functional testing asks:

How Does The Tumour Behave?

- drug sensitivity
- drug resistance
- biological response

This is hugely relevant.

Because if every patient gets a different metabolic plan:

Perhaps validation starts with:

"Was the intervention biologically rational for that patient?"

VS

Rather than:

"Did every patient get the same intervention?"

> *"Precision oncology is not only about what is mutated. It is also about what is actionable for that individual tumour."*

OPTION 5

The N-of-1 Aggregation Model

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Personalised evidence, built one patient at a time

This is actually becoming increasingly respected scientifically.

Each patient:

- acts as their own control
- baseline collected
- interventions introduced
- trajectory tracked

Then:

Hundreds of N-of-1 studies aggregated.

This sits between:

anecdote → **N-of-1 aggregation** → RCT

And is probably closer to how personalised medicine actually functions.

> *"Perhaps personalised medicine requires personalised evidence generation."*

Five Possible Futures

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Model	Strength	Weakness
Classical RCT	High rigour	Poor real-world representation
Registry Studies	Real-world	Confounding
AI Learning Systems	Handles complexity	Governance challenges
Functional Testing	Personalised biology	Requires validation
N-of-1 Aggregation	Reflects individuality	Novel methodology

No single model is perfect. The future may involve combining them.

THANK YOU

Appendix

VEGF (VEGFA ICC Positive & VEGFB Overexpression) Overexpression

- Luteolin
  - Luteolin Pro Liposomal, 150 mg - MCS Formulas
  - 1 capsule 2 x per day

- Ibuprofen

VEGFR1 (VEGFR1 ICC Positive) Overexpression

- Apigenin
  - Apigenin Pro Liposomal, 200 mg - MCS Formulas
  - 1 capsule 2 x per day
- EGCG
- Resveratrol
- Berberine –Dihydroberberine
- Curcumin

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VEGFR2 (VEGFR2 ICC Positive) Overexpression

- Resveratrol
- Apigenin

TP53 Missense

- Quercetin
- Metformin
- Lovastatin / Atorvastatin
- Fisetin
  - Fisetin Pro Liposomal, 150 mg - MCS Formulas
- Luteolin
  - Luteolin Pro Liposomal, 150 mg - MCS Formulas

BRCA1, Germline mutation - Missense

- Simvastatin
- Lovastatin

PI3K (KEGG Overexpression) Overexpression

- Carozolol / Propranolol
- Berberine consider Dihydroberberine
- Lovastatin / Atorvastatin
- Metformin

NOTCH1 (KEGG Overexpression) Overexpression

- Niclosamide
  - 500mg Twice a day
- Metformin
- Berberine – consider Dihydroberberine

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RAS/MEK/ERK (MAPK Pathway Activation) Overexpression

- Aspirin
- Minocycline = Doxycycline
- Myricetin (antioxidant flavonoid)
  - Source Naturals brand
- Ursolic acid
  - Glutamine Inhibifour, 120 Capsules - MCS Formulas
- Simvastatin / Atorvastatin

EGFR (EGFR ICC Positive) Overexpression

- Canagliflozin – this is an SGLT-2 inhibitor used for T2 Diabetes
  - Could consider at low dose as safe to use with Metformin without risk of hypoglycaemia
- Curcumin
- Mesalazine – this is a drug used in inflammatory bowel disease
  - Logistically difficult
- Ibuprofen – preferably Flarin (Liposomal Ibuprofen) unless
- Telmisartan – this is an anti-hypertensive agent.
  - Logistically difficult

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HMGB1 Overexpression

- Chloroquine
  - Could consider Hydroxychloroquine (lower side effect risk) – to discuss
- Metformin

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MMP Overexpression

- Doxycycline – already considered

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ESR1 Overexpression

- EGCG
- Berberine – Dihydroberberine
- Curcumin

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CCND1 Amplification

- Aspirin
- Metformin
- Quercetin
- Sulforaphane
  - Broccoli Ultra - MEGA dose of Sulforaphane

NFKB (KEGG Pathway Overexpression) Overexpression

- Curcumin
- Sulforaphane
  - Broccoli Ultra - MEGA dose of Sulforaphane
- Resveratrol
- Metformin
- Lycopene
  - Lycopene Plus, 38mg/Capsule - MCS Formulas