Metabolic Profile of Inflammatory Breast Cancer: aiding diagnosis and treatment

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Metabolic Profiling in simple terms.

- In a salad bowl, put the egg yolks and mix them with a whisk.
- Add the sugar to the yolks and mix until the mixture gets clearer.
- Add the cream, then the milk, and leave for 30 minutes.

**Pre-heat oven at 160°C / 310°F** and put 1 cm (1/2 in.) high water in the oven baking tray.

**Bake for about 10 minutes**; the cream must get thicker but stay soft; it must not get too brown.
- When baked, let them get cooler, then put in fridge for at least 1 hour.

**Last step, the "burning"** (sugar crust on top), just before serving:
- Pre-heat oven on grill position; evenly spread the brown sugar on the 4 creams then put under grill for just a few minutes (3 to 5, it is quick); the sugar will melt and get caramelized, don't let it burn!

**Serve right away** (hot on top, cold inside).
In the making
Crème Brulée

Tracer
[1,2-$^{13}$C$_2$]glucose tracer

Tumor cell

Glucose-1P $\rightarrow$ Glycogen

Ribose – DNA/RNA

Fructose-6P

Glyceraldehyde-3P

Lactate - Pyruvate

Acetyl-CoA

Krebs cycle

citric acid

$\alpha$-ketoglutarate glutamate

Lipid synthesis

Plasma membrane

Amino acids

Proteins

$^{13}$C Lactate

$^{13}$C Glutamate

$^{13}$C Ribose & DOR

$^{13}$C Fatty Acids

$^{13}$C Amino Acids
Glycolysis

Phosphoglucone isomerase

Phosphofructokinase

Aldolase

Phosphate Isomerase

Glyceraldehyde-3P
Glycolysis

[2,3-13C]dihydroxyacetone-P

[2,3-13C]glyceraldehyde-3P

[2,3-13C]pyruvate

Triose Phosphate Isomerase

Lactate dehydrogenase

[2,3-13C]lactate

RELEASED INTO CULTURE MEDIUM

m/z 328 Lact
DRUG TREATMENTS

AVEMAR

GLYCOGEN PHOSPHORYLASE INHIBITOR

2-DEOXY-D GLUCOSE
**A**
UNTREATED IBC CELLS

Glycogen → G1P → Glucose 
↓
G6P → RIBOSE
↓
F6P → GAP
↓
PDH
↓
OAA → Acetyl-CoA → FATTY ACIDS
↓
?-ketoglutarate
↑
GLUTAMATE

**B**
CPD TREATED IBC CELLS

Glycogen → G1P → Glucose 
↓
G6P → RIBOSE
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F6P → GAP
↓
PDH
↓
OAA → Acetyl-CoA → FATTY ACIDS
↓
?-ketoglutarate
↑
GLUTAMATE

Apoptosis / IBC cell death
Effect of 10 mg/ml Avemar (24h) on de novo fatty acid synthesis

Average of 5.746 to 5.945 min.: 2302045.D

Time-->
B

**Total RNA ribose $^{13}$C accumulation from glucose**

- **13C enrichment in total cell RNA ($\sum m_n$)**

<table>
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<th>C</th>
<th>50</th>
<th>75</th>
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<td><strong>5 GPI</strong></td>
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<td>(microM)</td>
<td>0.7</td>
<td>0.6</td>
<td>0.5</td>
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<th>1.0</th>
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<td><strong>Avemar</strong></td>
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**De novo** palmitate synthesis

Acetyl-CoA $^{13}$C enrichment from glucose

![Bar chart showing](chart.png)

Per cent of total

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![Bar chart showing](chart2.png)

**De novo** palmitate synthesis

Acetyl-CoA $^{13}$C enrichment from glucose

![Bar chart showing](chart3.png)

Per cent of total

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**De novo** palmitate synthesis

Acetyl-CoA $^{13}$C enrichment from glucose

![Bar chart showing](chart4.png)

Per cent of total

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Control IBC cells

Glucose → NADPH → RIBOSE
G6P → G6PDH
F6P → TRANSKETOLASE
GAP → PDH
LACTATE ↔ PYR
OAA → Acetyl-CoA → FATTY ACIDS
?-ketoglutarate ↔ GLUTAMATE

Avemar treated IBC cells

Glucose → NADPH → RIBOSE
G6P → G6PDH
F6P → TRANSKETOLASE
GAP → PDH
LACTATE ↔ PYR
OAA → Acetyl-CoA → FATTY ACIDS
?-ketoglutarate ↔ GLUTAMATE

Decreased proliferation
Deoxyglucose Inhibition on IBC

- **% of Survival Cells**
- **Con.(mM)**
- **24hrs inhibition**
- **72hrs inhibition**

- **con**
- **1mM**
- **2mM**
- **5mM**
STUDY RESULT

SUMMARY

• IBC cells have a very unique metabolic profile.

• They are sensitive to DOG and Avemar treatment
AGENDA

• DIAGNOSTIC TEST BASED ON METABOLIC PROFILE AND TRACER TECHNIQUE

• NEW TREATMENT TARGETING UNIQUE METABOLIC ENZYMES
THANKS TO

- **IBC RESEARCH FOUNDATION**
- **HARBOR UCLA RESEARCH FACILITIES**