An abstract model of the metabolism regulation of pancreatic ductal adenocarcinoma

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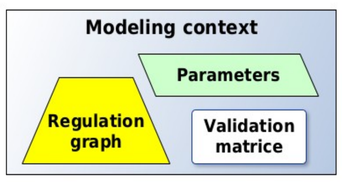
Introduction

The tissue organisation of the pancreas gives the cells a particular resistance. Indeed, this very confined environment makes the supply of nutrients lower and their metabolism more adapted to survive these conditions. Biologists assume that the aggressiveness of pancreatic ductal adenocarcinoma (PDAC) may be related to this cellular ability to adapt its metabolism [1].

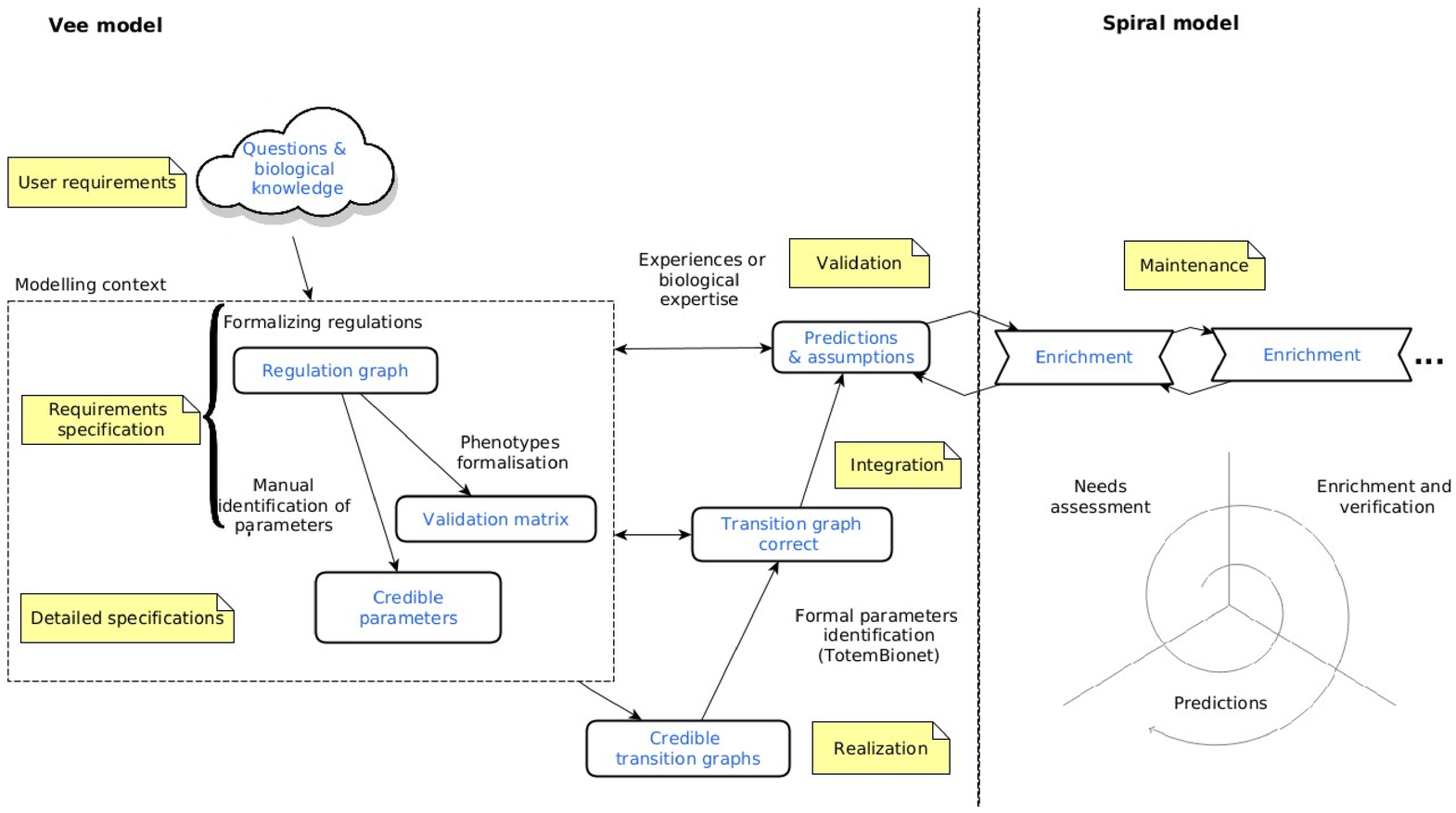
Aims to **discover and understand the regulation of metabolism involved in cancer progression.**

Aims to **develop a coarse-grained model of metabolic regulations and simulate possible regulations [2].**

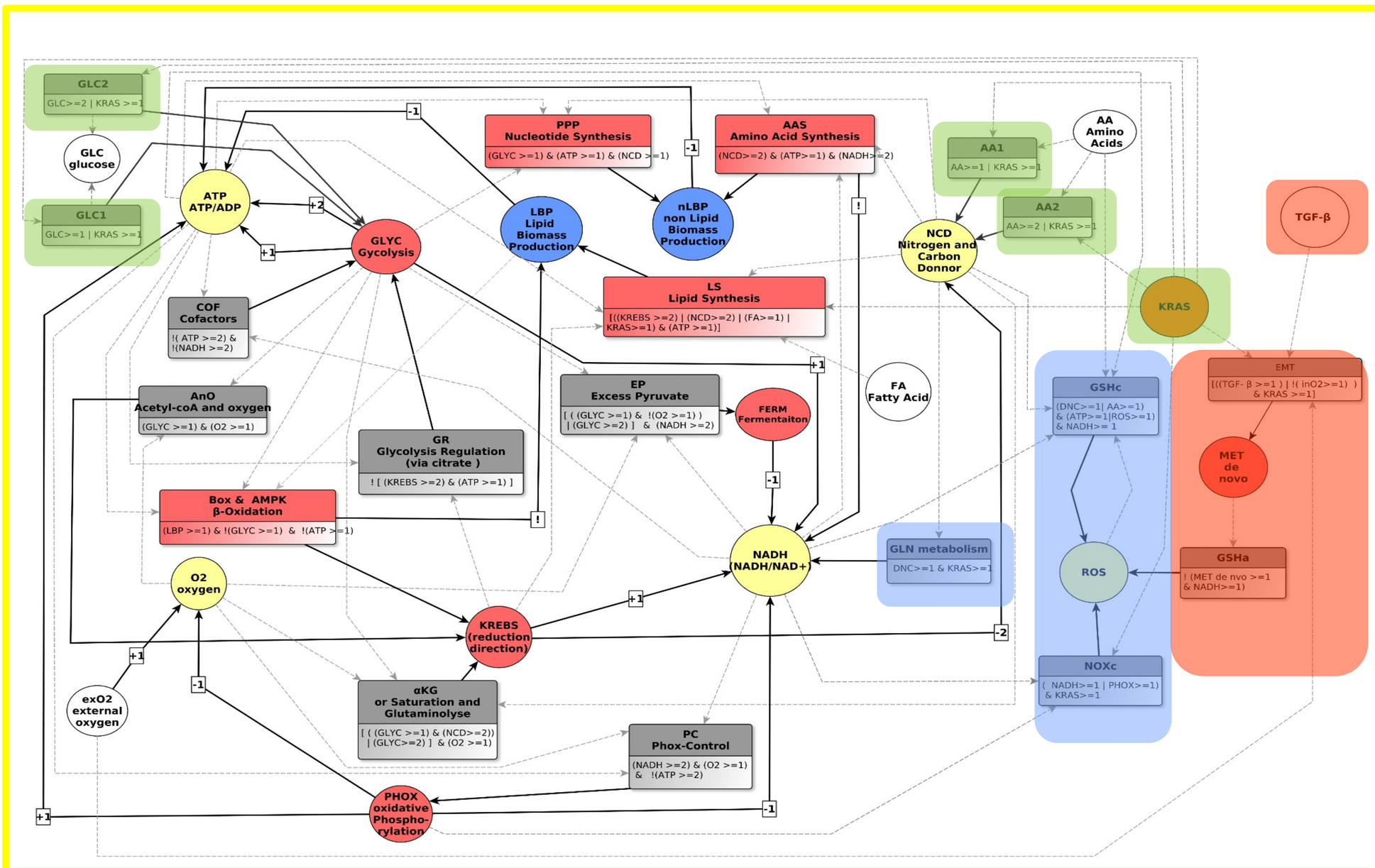


Aim of coarse-grained model: Focus on the cooperation on well known pathways.

Modeling methodology [3]



Modeling context [4]



Enrichment steps

- Genetic context addition
- Specialisation to cancer
- Specialisation to agressive cancer

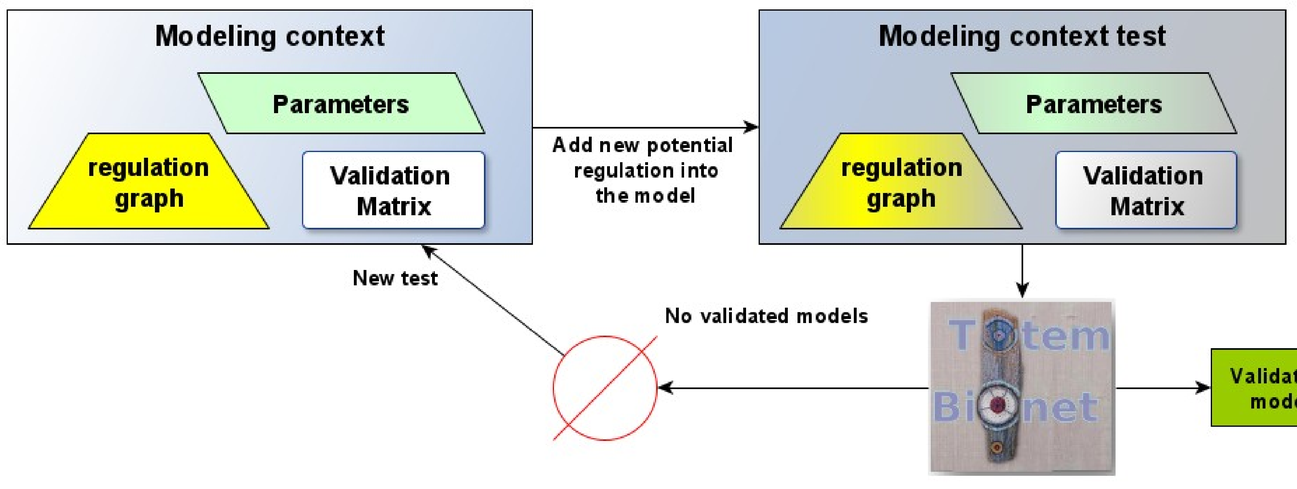
Parameters

K_GLYC:GLC1
K_GLYC:COF
K_FERM
K_FERM:EP
…
K_ROS:GSHc
…
K_MET:EMT

Validation Matrix

Environment		Attempted phenotypes	
GLC & FA & exO2 & AA & KRAS & TGF-B		GLYC	ROS
• GLC=1 • FA=0 • AA=1	• exO2=2 • KRAS=0 • TGF-β=0	Osc	Td(0)
• GLC=1 • FA=0 • AA=1	• exO2=2 • KRAS=1 • TGF-β=0		Td(2)
• GLC=1 • FA=0 • AA=1	• exO2=2 • KRAS=1 • TGF-β=1		Td(1)

Test hypotheses on regulations



Tested & validated regulations:
Met de novo → Lipid synthesis
Met de novo → PPP

Biology in progress…

Bibliography

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