#3523: PREDICTIVE MODELS OF RECURRENCE FROM TRANSCRIPTOMIC SIGNATURES OF THE TUMOR MICROENVIRONMENT AND CELL CYCLE IN STAGE III COLON CANCER FROM PETACC-8 AND IDEA-FRANCE TRIALS

Gallois C[1,2], Sroussi M[1,3], André T[4], Mouillet-Richard S[1], Agueeff N[1], Vernerey D[5], Louvet C[6], Bachet JB[7], Dourthe LM[8], Mazard T[9], Jary M[10], de la Fouchardiere C[11], Lecaille C[12], Tabernero J[13], Van Laethem JL[14], Lepage C[15], Emile JF[16], de Reynies A[1], Taieb J[1,2] and Laurent-Puig P[1]

1- Paris Université, INSERM, Université Paris Cité, France, 2-Institut du Cancer Paris CARPEM, APHP, Digestive Oncology Department, APHP.Centre, Université Paris Cité, Hôpital Européen G. Pompidou, France, 3-Institut Chimie Biologie Innovation – Laboratoire de BioChimie, ESPCI, UMR8231 CNRS, Université PSL, Paris, France, 4- Sorbonne Université and Hôpital Saint Antoine, Paris, France, 5- Methodology and Quality of Life Unit in Oncology, University of Besançon, Besançon, France, 6- Department of Medical Oncology, Institut Mutualiste Montsouris, Paris, France, 7- Sorbonne Universités, UPMC Université, Department of Gastroenterology, Pitié-Salpetriére Hospital, Paris, France, 8-Department of medical oncology, Clinique Saint-Anne, Strasbourg, France, 9 - Institut Régional du Cancer de Montpellier (ICM), INSERM, University of Montpellier, France, 10 - Department of Digestive and Hepatobiliary Surgery, Hôtel Dieu, Clermont-Ferrand, France, 11 - Department of Medical Oncology, Centre Leon Berard, University Claude Bernard Lyon Lyon, France 12 - Cancerology Department, Bordeaux Nord Polyclinic, Bordeaux, France, 13 - Vall d'Hebron University Hospital (HUVH) and Institute of Oncology (VHIO), IOB-Quiron, UVic-UCC, Barcelona, Spain, 14 - Departement of Digestive Oncology, HUB, Université Libre de Bruxelles, Belgium, 15-Hepatogastroenterology and Cancerology Department, Dijon Bourgogne Hospital, University entre de Recherche des Cordeliers, Sorbonne of Burgundy and Franche Comté, Dijon, France, 16 - EA4340 BECCOH, Université de Versailles SQY, Service de Pathologie, Hôpital Ambroise Paré, AP-HP, Boulogne, France.

Objectives:

→to establish a **predictive model of the risk of recurrence** in **stage III colon cancer** (CC) based on transcriptomic signatures of the tumor microenvironment (TME) and cell cycle from the PETACC-8 and IDEA- France trials.

Methods:

3'RNAseq*

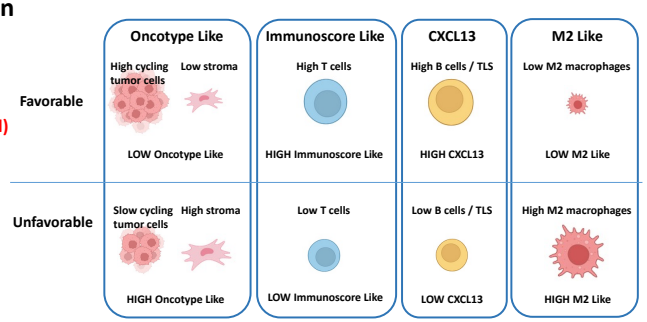
*QuantSeq 3'mRNA-Seq Kit FWD for Illumina (Lexogen™), NovaSeq6000 (Illumina))

PETACC-8	IDEA-France
N=1733	**N=1263**
training set	validation set

4 genomic signatures of TME and cell cycle

- **Immunoscore Like signature** (*Marisa et al. JNCI 2018*)
  → *CD3E,CD3G, CD3D,CD8A* and *PTPRC*
- **Oncotype Like score**: derived from the Oncotype DX® Colon Cancer RS (*O'Connell et al. JCO 2010)*:
  . stromal score = *BGN*, *FAP* and *INHBA*
  . cell cycle score =*MKi67*, *MYC* and *MYBL2*
  Oncotype Like score = 44 x ((0.15 × stromal score − 0.30 × cell cycle score + 0.15 × gene expression of *GADD45B*)+0.82)
- **Macrophage M2 Like signature** (*Combes et al. Cell 2022*)
- **CXCL13 expression**

IPS score
(Immune Proliferative Stromal)
= **number of unfavorable signatures**
(0 to 4)

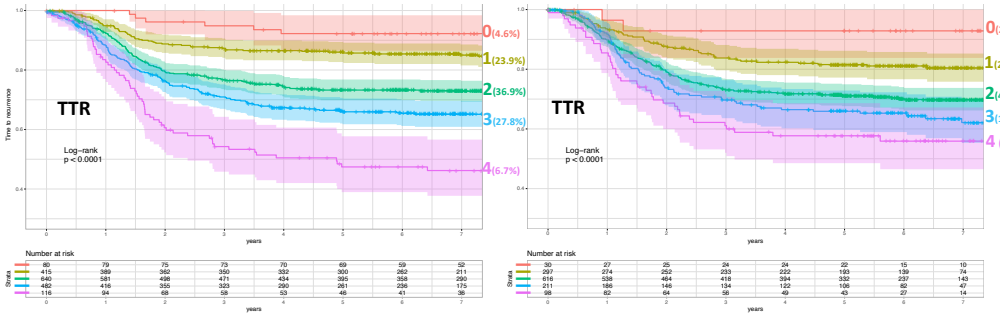


In stage III colon cancer:
3'RNAseq signatures related to:
→T cells
→B cells/TLS
→Macrophages M2
→Stroma
→Cell cycle
provide important information for patient stratification on risk of recurrence

pierre.laurent-puig@parisdescartes.fr

Results

TTR according to IPS score



PETACC-8 trial **IDEA-France trial**

Multivariate models

	PETACC-8		IDEA-France	
	adj HR	p	adj HR	p
T4	2.0	**<0.01**	1.6	**<0.01**
N2	2.2	**<0.01**	2.4	**<0.01**
IPS score				
1	1.8	0.2	2.3	0.2
2	3.4	**<0.01**	3.9	**0.058**
3	4.4	**<0.01**	4.6	**0.03**
4	6.7	**<0.01**	5.7	**0.02**
Dismal CMS combination	1.6	**<0.01**	1.1	0.5
Treatment duration: 3 months			1.5	**<0.01**

Future Directions for Research:

Beyond T and N stage, for the decision of adjuvant chemotherapy in stage III CC, the combination of these different variables could be exploited in the future for personalized care (de-escalation, intensification), or stratification in therapeutic trials

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