The Link Between the Immune Microenvironment and Outcome in Colorectal Cancer

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Disclosures

Co-founder and chairman of the scientific advisory board:
  - HalioDx

Collaborative Research Agreement (grants): 
  - Perkin-Elmer, IObiotech, MedImmune, Janssen, Imcheck Therapeutics

Participation to Scientific Advisory Boards:
  - BMS, MedImmune, Astra Zeneca, Novartis, Definiens, Merck Serono, IObiotech, ImmunID, Nanostring, Illumina, Northwest Biotherapeutics, Actelion, Amgen, Merck MSD

Consultant:
  - BMS, Roche, GSK, Compugen, Mologen, Gilead, Sanofi
Cancer is one of the most complex biological system of all.

“The whole is greater than the sum of its parts”, Aristotle

\[ \rightarrow \text{Systems biology in human cancer} \]
What is the importance of the pre-existing immunity within tumors? Does it matter?

Cancer patient

Current cancer classification
Tumor cell characteristics

Tumor cell extension and invasion
Anatopathology
Tumor Morphology
Tumor cell of origin
Tumor Molecular pathway
Tumor Gene expression
Tumor Mutation status

Immune-based classification
Host immune response

Currently NONE

T-stage
N-stage
M-stage
Grade
Budding
Etc...
Stem cell
Goblet cell
Etc...
MSI
CIN
Etc...
CMS
Etc...
PS3
KRAS
BRAF
Etc...
A Novel Paradigm for Cancer

Type, Density, and Location of Immune Cells Within Human Colorectal Tumors Predict Clinical Outcome

Jérôme Galon,† Anne Costes,† Fatima Sánchez-Cabo, Amos Kirilovsky, Bernhard Mäenik, Christine Lagorce-Pagès, Marie Tosolini, Matthieu Camus, Anne Berget, Philippe Wind, Franck Zinzindohoué, Patrick Brunet, Paul-Henri Cugnenc, Zlatko Trajanoski,
Wolfgang-Friedman,†‡ Franck Pagès‡,†

29 SEPTEMBER 2006 VOL 313 SCIENCE www.sciencemag.org

- Gene expression profiling
- Qualitative immune signature

- Immunohistochemistry (IHC)
- Digital Pathology
- Quantitative immune cell infiltration

Optimized Immunosign Quality

Type/Density/Location

Galon J et al. Science 2006
Coordinated adaptive immune reaction (Immunoscore) more than tumor invasion predicts clinical outcome

Galon et al. Science 2006
## A Novel Paradigm for Cancer

### Multivariate Cox Analysis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-stage</td>
<td>1.2</td>
<td>0.25</td>
</tr>
<tr>
<td>N-stage</td>
<td>1.4</td>
<td>0.15</td>
</tr>
<tr>
<td>Differentiation</td>
<td>1.1</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Immunoscore</strong></td>
<td>1.9</td>
<td>0.00001</td>
</tr>
</tbody>
</table>

#### “Immune Contexture”:

- Cells ->
  - Type
- Quantity ->
  - Density
- Spatial ->
  - Location
- Quality ->
  - Immune **functional** orientation

-> Immunoscore

-> Immunosign

Cox Multivariate analysis including Immunoscore

<table>
<thead>
<tr>
<th>COX analysis for DPS</th>
<th>HR</th>
<th>Log Rank P-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor (T) stage</td>
<td>1.24</td>
<td>0.29</td>
</tr>
<tr>
<td>N Stage</td>
<td>1.31</td>
<td>0.17</td>
</tr>
<tr>
<td>Gender</td>
<td>1.47</td>
<td>0.18</td>
</tr>
<tr>
<td>Number of total Lymph nodes</td>
<td>1.13</td>
<td>0.68</td>
</tr>
<tr>
<td>Histological grade</td>
<td>0.69</td>
<td>0.29</td>
</tr>
<tr>
<td>Mucinous Colloide</td>
<td>1.29</td>
<td>0.47</td>
</tr>
<tr>
<td>Occlusion</td>
<td>1.03</td>
<td>0.94</td>
</tr>
<tr>
<td>Perforation</td>
<td>4.03</td>
<td>0.0084</td>
</tr>
<tr>
<td><strong>Immunoscore</strong></td>
<td>0.65</td>
<td><strong>0.0003</strong></td>
</tr>
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</table>

TNM Staging in Colorectal Cancer: T Is for T Cell and M Is for Memory

Elizabeth K. Broussard and Mary L. Daise, Tumor Vaccine Group, Center for Translational Medicine in Women's Health, University of Washington, Seattle, WA

Histopathologic-Based Prognostic Factors of Colorectal Cancers Are Associated With the State of the Local Immune Reaction

Bernhard Mlecnik, Marie Tourni, Anton Kirilovsky, Anne Berger, Gabriela Beredo, Tadashi Nishida, Patrice Brunner, Zbigniew Ptaszynski, Wolf-Hermann Fehmann, Frans Pagel, and Jerome Galon

"TNM staging: T is for T cell and M is for Memory"

Editorial: Broussard et al. JCO 2011

Multivariate Analysis

<table>
<thead>
<tr>
<th></th>
<th>DFS</th>
<th>OS</th>
<th>DSS</th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>P-value</td>
<td>HR</td>
</tr>
<tr>
<td>AJCC/UICC-TNM</td>
<td>1.38</td>
<td>0.09 ns</td>
<td>1.18</td>
</tr>
<tr>
<td><strong>Immunoscore</strong></td>
<td><strong>0.64</strong></td>
<td><strong>&lt;0.0001</strong></td>
<td><strong>0.71</strong></td>
</tr>
</tbody>
</table>

Galon et al. Science 2006, Mlecnik et al. JCO 2011

✓ An immune classification of cancer
✓ The power of the pre-existing immunity
✓ The possibility to unleash the immune response with immunotherapy
Immunoscore in early-stage (I/II) colorectal cancer

In Situ Cytotoxic and Memory T Cells Predict Outcome in Patients With Early-Stage Colorectal Cancer
Franck Pages, Amos Kirilovsky, Bernhard Mlecnik, Martin Asslaber, Marie Tosolini, Gabriela Bindea, Christine Lagorce, Philippe Wind, Florence Marliot, Patrick Bruneval, Kurt Zatloukal, Zlatko Trajanoski, Anne Berger, Wolf-Herman Fridman, and Jérôme Galon

J Clin Oncol. 27, 5944-51 (2009)
Prognostic importance of the *in situ* immune reaction in patients with early-stage (Stage I/II) colorectal cancer

Evaluation in the Center (CT) and the Invasive margin (IM) of the tumor
Cohort 1 = 411 patients, cohort 2 = 188 patients

**CD45RO<sub>CT/IM</sub> CD8<sub>CT/IM</sub>**

P<0.0001

- **(4)-Hi** 42% 1
- **(3)-Hi** 27% 2.9
- **all patients**
- **(1-2)-Hi** 27% 10.2
- **(0)-Hi** 4% 23.1

**COX multivariate analysis**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-stage</td>
<td>1.2</td>
<td>0.41</td>
</tr>
<tr>
<td>Perforation</td>
<td>5.5</td>
<td>0.003</td>
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<tr>
<td>Immune pattern</td>
<td>0.3</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

Understanding the evolution of the immune response with tumor progression using systems biology

- The Immune Landscape in human cancer
- Evolution of the tumor microenvironment with tumor progression?
- Immune escape mechanisms in human tumors?

-> Spatio-temporal dynamics of the immune response with tumor progression

Bindea G et al. *Immunity*, 2013
What are the mechanistic relationships between tumor genotype and Immunoscore?

Integrative Analyses of Colorectal Cancer Show Immunoscore Is a Stronger Predictor of Patient Survival Than Microsatellite Instability

Bernhard Mlecnik,1,2,3,19 Gabriela Bindea,1,2,3,15 Helen K. Angell,1,2,3,4 Pauline Maby,1,2,3,5 Mihaela Angelova,1,2,3,6 David Tougeron,5,7,8 Sarah E. Church,1,2,3 Lucie Lafontaine,1,2,3 Maria Fischer,9 Tessa Fredriksen,1,2,3 Maristella Sasso,1,2,3 Amélie M. Bilocq,1,2,3 Amos Kirilovsky,7 Anna C. Obenauf,9 Mohamad Hamieh,5 Anne Berger,1,10 Patrick Bruneval,11 Jean-Jacques Tuch,11 Jean-Christophe Sabourin,15 Florence Le Pessot,15 Jacques Maullion,13,14 Arash Rafii,15 Pierre Laurent-Puig,2,16 Michael R. Speicher,9 Zlatko Trajanoski,9 Pierre Michel,7 Richard Sesboüe,3 Thierry Frebourg,5,16 Franck Pages,1,2,3,17 Viia Valge-Archer,4,18 Jean-Baptiste Latouche,5,8 and Jérôme Galon1,2,3,14

TCGA CRC cohort: n = 270 patients

Inserm cohort: n = 689 patients

Mlecnik et al. *Immunity* 2016
Mechanistic impact of DNA-mismatch repair deficiency

Increased frequency of Frameshift mutations

Increased Proliferating T-cells, Th1, cytotoxic T-cells

Anti-TGFBR2mutFS Specific T-cells

Genetic evidence of Immunoediting

Increased frequency of High-Immunoscore

CRC cells

Mlecnik et al. *Immunity* 2016
Immunoscore high (I3, I4) patients have prolonged survival regardless of the MSI status.

Cox multivariate analysis for DSS

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>MSI</td>
<td>1.00</td>
<td>0.99</td>
</tr>
<tr>
<td>N stage</td>
<td>1.32</td>
<td>0.27</td>
</tr>
<tr>
<td>VELIPI</td>
<td>0.56</td>
<td>0.024 *</td>
</tr>
<tr>
<td>Immunoscore</td>
<td>0.44</td>
<td>0.001 *</td>
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</table>

Mlecnik et al. Immunity 2016
# Colorectal cancer classifications

<table>
<thead>
<tr>
<th>Tumor cell extension and invasion</th>
<th>T-STAGE</th>
<th>N-STAGE</th>
<th>M-STAGE</th>
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</thead>
<tbody>
<tr>
<td>Ways to classify</td>
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<tr>
<td>Morphology</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mucinous</td>
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<td></td>
<td></td>
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<tr>
<td>Medullary</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Adeno. NOS</td>
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<td></td>
<td></td>
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<tr>
<td>Serrated</td>
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<tr>
<td>Signet ring cell</td>
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<td></td>
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<tr>
<td>Micropapillary</td>
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<tr>
<td>Cribriform comedolike</td>
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<tr>
<td>Tumor cell characteristics</td>
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<tr>
<td>Cell of origin</td>
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<tr>
<td>Enterocyte</td>
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<tr>
<td>Goblet-like</td>
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<td></td>
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<tr>
<td>Transit-amplifying-R</td>
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<tr>
<td>Transit-amplifying-S</td>
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<tr>
<td>Inflammatory</td>
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<tr>
<td>Stem-like</td>
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<tr>
<td>Host immune response</td>
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<tr>
<td>Immunoscore</td>
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<td></td>
<td></td>
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<tr>
<td>CD3+ T cells</td>
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<tr>
<td>CD8+ T cells</td>
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<tr>
<td>Density</td>
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</tr>
<tr>
<td>Location (CT, IM)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Galon et al. J Pathol. 2014
The Immunoscore as a New Possible Approach for the Classification of Cancer

World Immunotherapy Council inaugural meeting (Feb 2012)

Support (moral) from the World Immunotherapy Council (WIC), and support from societies including, EATI, BDA, CCIC, CIC, CRI, CIMT, CSCO, TIBT, DTIWP, ESCII, NIBIT, JACI, NCV-network, PIVAC, ATTACK, TVACT...

Worldwide Immunoscore consortium (PI: J Galon)
(17 countries: >3000 Stage I/II/III Colon cancer patients)

Assay harmonization

Immunoscore meetings:
- Feb 2012, Italy
- Dec 2012, Italy
- Nov 2013, SITC, USA
- Dec 2013, Italy
- Jan 2014, Qatar
- Jul 2014, Paris, France
- Nov 2014, SITC, USA
- Nov 2015, SITC, USA
- Dec 2015, Italy
- Feb 2016, USCAP, USA
- April 2016, USA
- Nov 2016, SITC, USA
- Dec 2016, Italy
- Feb 2017, USCAP, USA
- Dec 2017, Italy
International validation of the consensus Immunoscore for the classification of colon cancer: a prognostic and accuracy study

Relative variable contribution to risk

Chi squared proportion ($\chi^2$) test for clinical parameters

Cox Multivariate

<table>
<thead>
<tr>
<th>Immunoscore</th>
<th>P-values</th>
<th>c-index</th>
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</thead>
<tbody>
<tr>
<td>2 groups</td>
<td>&lt;0.0001</td>
<td>0.73 (0.66-0.80)</td>
</tr>
<tr>
<td>3 groups</td>
<td>&lt;0.0001</td>
<td>0.73 (0.67-0.80)</td>
</tr>
<tr>
<td>5 groups</td>
<td>&lt;0.0001</td>
<td>0.73 (0.67-0.80)</td>
</tr>
</tbody>
</table>

Pages et al. The Lancet 2018
Immunoscore in locally advanced colon cancer

Stage III
Immunoscore in locally advanced colon cancer

Stage III

Immunoscore prognostic value:

✓ HEGP, Paris France cohort
✓ SITC, worldwide study
✓ N0147 phase 3 clinical trial
✓ IDEA, France, phase 3 clinical trial

✓ Predefined cut-off from Worldwide SITC study, and Predefined statistical plan (Mayo Clinic)
✓ 4 independent cohorts, 2514 patients
Phase 3 randomized study of stage III colon cancer patients (IDEA) 3 vs 6 months of chemotherapy (n=1062)

Immunoscore (2 groups)

- IS High (Hi+Int): 599 (56.54%)
- IS Low: 463 (43.6%)

HR = 1.54 (95CI% 1.24-1.93), P < 0.0001

Immunoscore (3 groups)

- IS Hi: 100 (9.4%)
- IS Int: 499 (47.0%)
- IS Low: 463 (43.6%)

HR = 2.42 (95CI% 1.47-3.99), P < 0.0001

Demonstration of the **Prognostic** value of Immunoscore in a randomized cohort of Stage III colon cancer patients

ASCO 2019
Immunoscore in stage III colon carcinoma patients

- Predefined cut-off from Worldwide SITC study, and Predefined statistical plan (Mayo Clinic)
- 4 independent cohorts, 2514 patients

Immunoscore predicts High-risk and No-risk patients in stage III colon cancer
Immunoscore in locally advanced colon cancer

Stage III

Immunoscore Predictive value:

✓ IDEA, France, phase 3 clinical trial (3 months vs 6 months chemotherapy)
Phase 3 randomized study of stage III colon cancer patients (IDEA) 3 vs 6 months of chemotherapy (n=1062)

All Stage III treated with FOLFOX

High Immunoscore

- HR = 0.53 (95% CI 0.37-0.75)
- P = 0.0003

Low Immunoscore

- HR = 0.84 (95% CI 0.61-1.15)
- P = 0.27

High Immunoscore significantly predicts response to 6 months FOLFOX chemotherapy in all Stage III patients.
Phase 3 randomized study of stage III colon cancer patients (IDEA) 3 vs 6 months of chemotherapy (n=1062)

Low-Risk (T1-3 and N1)

High Immunoscore

HR=0.47 (95CI% 0.26-0.83), P=0.01

Low Immunoscore

HR=0.86 (95CI% 0.52-1.42), P=0.56

High Immunoscore significantly predicts response to 6 months FOLFOX chemotherapy in Low-Risk Stage III patients

ASCO 2019
Phase 3 randomized study of stage III colon cancer patients (IDEA) 3 vs 6 months of chemotherapy (n=1062)

High-Risk (T4 or N2)

High Immunoscore

Low Immunoscore

**High Immunoscore significantly predicts** response to 6 months FOLFOX chemotherapy in High-Risk Stage III patients

ASC0 2019
International consensus Immunoscore SITC study: Stage III colon cancer patients treated or not treated with chemotherapy

High Immunoscore

Low Risk, Immunoscore Int+Hi (25-100%) Chemotherapy

- NO
- YES

$P < 0.001$

Low Immunoscore (10)

Low Risk, Immunoscore 10 (0-10%) Chemotherapy

- NO
- YES

$P = 0.83$

High Immunoscore significantly predicts response to chemotherapy in Stage III patients
Conclusions: Stage III colon cancer patients

Immunoscore is a significant \textit{prognostic} marker of survival in Stage III patients \textit{(Science 2006, J Clin Oncol 2011)}

Immunoscore is a significant \textit{prognostic} consensus marker of survival in Stage III patients \textit{(Lancet 2018, NO147 study, IDEA study)}

\textbf{High} Immunoscore is significantly \textit{predictive} of response to chemotherapy in Stage III colon cancer patients \textit{(SITC study)}

\textbf{High} Immunoscore is significantly \textit{predictive} of response to 6 months FOLFOX chemotherapy in Stage III colon cancer patients \textit{(IDEA study)}

\textbf{Low} Immunoscore patients \textit{do not respond} to chemotherapy \textit{(SITC study)}

nor to 6 months FOLFOX chemotherapy in Stage III colon cancer patients \textit{(IDEA study)}
Is there an immune escape at the metastatic stage?

Stage IV
Metastasis analysis

One primary tumor
Colorectal cancer

Multiple metastatic sites
Liver Metastasis
Lung Metastasis

N=603 metastases

- Immunoscore within multiple metastases at different sites

Mlecnik et al. JNCI 2018
Metastasis analysis

The Link between the Multiverse of Immune Microenvironments in Metastases and the Survival of Colorectal Cancer Patients

Marc Van den Eynde, Bernhard Mlecnik, Gabriele Bindea, Tessa Fredriksen, Sarah E. Church, Lucie Lafontaine, Nacilla Haicheur, Florence Marlot, Mihaela Angelova, Angela Vasaturo, Daniela Bruni, Anne Journot-Mourin, Pamela Baldin, Nicolas Huyghes, Karin Haustermanns, Amelies Debecquey, Eric Van Cutsem, Jean-Francois Gigot, Catherine Hubert, Alex Kartheuser, Christophe Remue, Daniel Léonard, Vila Valge-Archer, Franck Pagès, Jean-Pascal Machiels, and Jérôme Galon

➤ Immunoscore within multiple metastases at different sites

Van den Eynde et al. Cancer Cell 2018
What drives metastasis?

What are the metastatic escape mechanisms?

A Novel theory of cancer evolution?
Current theories of cancer evolution

Models

- LINEAR
- NEUTRAL
- BIG-BANG
- BRANCHED

Immune pressure from Darwinian selection

- NO
- NO
- NO
- NO

- The 4 proposed theories of cancer evolution
- All theories are tumor cell-centric. None involves a role of the immune system.
Evolution of Metastases in Space and Time under Immune Selection

Mihaela Angelova, Bernhard Mlecnik, Angela Vasaturo, Gabriela Bindea, Tessa Fredriksen, Lucie Lafontaine, Bénédicte Buttard, Erwan Morgand, Daniela Bruni, Anne Jouret-Mourin, Catherine Hubert, Alex Kartheuser, Yves Humbert, Michele Ceccarelli, Najeel Syed, Francesco M. Marincola, Davide Bedognetti, Marc Van den Eynde, and Jérôme Galon

Angelova M. et al. Cell 2018
What drives metastasis?

Primary tumors
- Synchronous metastases
- Metachronous metastases
- Metachronous metastases

Multi-Omics technologies

Chromosomal Instability
Tumor Genetics
- Tumor-gene expression
- Mutations

Vessels
Host Immune Microenvironment
Immune Cells
Genomics of primary tumors and metastases

✓ Highly heterogeneous genomic patterns between metastases
Evolvogram of tumor clones

✓ Clonal evolution and cancer evolvogram
✓ Non-recurrent clones are immunoedited. Progressing clones are immune privileged
Immune microenvironment

Immune cell densities (cells/mm\(^2\))

Spatial profiling

---

** ✓ Immunomics patterns and immune cell infiltration within metastases**

Angelova M. et al. *Cell* 2018
Multivariate analysis of all genomics and immunomics parameters

<table>
<thead>
<tr>
<th>Excluded variable</th>
<th>Df</th>
<th>First recurrence</th>
<th>Multiple recurrences</th>
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<tbody>
<tr>
<td>&lt;none&gt;</td>
<td></td>
<td>43.3</td>
<td>124</td>
</tr>
<tr>
<td>CD3 to CK+Ki67+ mutual neighbor distance</td>
<td>1</td>
<td>43.7</td>
<td>-2.2</td>
</tr>
<tr>
<td>Immunoscore (Hi)</td>
<td>1</td>
<td>46.2</td>
<td>-3.1</td>
</tr>
<tr>
<td>Immunoscore (&gt;60%)</td>
<td>1</td>
<td>48.1</td>
<td>-3.1</td>
</tr>
<tr>
<td>Meta Size (log)</td>
<td>1</td>
<td>45.9</td>
<td>2.5</td>
</tr>
</tbody>
</table>

- Cox multivariate analysis revealed 4 parameters associated with metastatic dissemination:
- Immunoscore, Immunoediting, the distance between CD3 T-cells and Ki67+ tumor cells, and the size of the parent metastasis
Validation Study

CRC Primary tumor recurrence (n=132 patients)

Immuoediting

Predictive model

> Immunoediting and Predictive model are predictive factors of recurrence.
What drives metastasis? Conclusions

Different escape mechanisms delineated by lack of adaptive immunity or immunoediting.

Angelova M. et al. Cell 2018
What drives metastasis? Conclusions (2)

- Multiverse of metastases evolution in space and time under immune selection
- Evolution of tumor clones is linked to the intra-metastatic immune contexture.
- Non-recurrent clones are immunoedited. Progressing clones are immune privileged.

Angelova M. et al. *Cell* 2018
What drives metastasis? Conclusions (3)

- Parallel selection model describes tumor evolution during the metastatic process.
- Immunoediting and Immunoscore are predictive factors of metastasis recurrence.
- Distance between CD3+ cells and tumor cells Ki67+ and metastasis size are also associated metastasis recurrence.

Angelova M. et al. Cell 2018
A Novel theory of cancer evolution

Models

LINEAR  NEUTRAL  BIG-BANG  BRANCHED  SELECTION

Immune pressure from Darwinian selection

NO  NO  NO  NO  YES

- Parallel immune selection model
- Dynamic interaction of tumor-cells with immune-cells and Darwinian selection of immune escape variant, with parallel evolution and multiverse of metastases.
Metastatic colorectal cancer patients: For clinical routine

Stage IV

Pathological score
- Steatohepatitis, HGP, NRH, TRG, R status, Number of lesions,

Molecular status
- RAS mutations

Immunoscore
- Consensus Immunoscore applied to metastases

Current

New
Metastatic colorectal cancer patients: For clinical routine

Chi squared proportion ($\chi^2$) test for clinical parameters: Relative contribution to the risk test

**Time to recurrence (TTR)**
- Pathological score (56%)
  - HR = 3.32
  - pVal < 0.001
- Immunoscore (43%)
  - HR = 0.39
  - pVal = ns
- RAS status (<1%)
  - HR = 1.71
  - pVal = ns

**Overall survival (OS)**
- Immunoscore (52%)
  - HR = 0.23
  - pV < 0.01
- RAS status
- Pathological score (24%)

- Among molecular status, pathological parameters and Immunoscore, only Immunoscore has a significant contribution to the risk of TTR and OS.
- Immunoscore has the highest contribution to the risk of death in metastatic disease.
Deciphering the tumor immune microenvironment:
Clinical implications

"Cold" Tumor I0

Clinical implications
Predictions
Need T-cell priming Cancer vaccine

"Hot" Tumor I4

Response to immunotherapies (CTLA4, PD1, PDL1, ...)

But it is not as simple since biology is complex and is not dichotomized in good & bad
Treating hot, altered and cold immune tumors with immunotherapy

Galon J. & Bruni D.
Nature Reviews Drug Discovery 2019
Approaches to treat immune hot, altered and cold tumours with combination immunotherapies

Jérôme Galon and Daniela Bruni

2019

- Absent: Low Immunoscore
  - Cold: Non-inflamed

- Altered: Intermediate Immunoscore
  - Excluded: CT-Lo, Hi-IM
  - Immunosuppressed

- Optimal: High Immunoscore
  - Hot: Inflamed

Response to T cell checkpoint inhibition
Stratification of cancer based on the immune status

Tumor classification

MSI-H A
MSS B
MSS/CIMP.hi C
MSS D
MSS-CIMP.lo E

Immune classification

IMMUNE

-> Importance of having standardized immune Assays
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