CONECTUS
FOURNISSEUR OFFICIEL D'INNOVATIONS

INNOVATIVE TECHNOLOGY

PREDMED

Clinical Decision Support solution for Solid Tumor

#e-Health #Cancer

E-Clinical Decision Support for precision oncology

PREDMED
Predict Efficacy

- Prediction of **the best cancer therapy** for each patients based on the **level of deregulation** of genes

+

Interoperable solution with other diagnostic & e-Health solutions

Context & Market size

- Advances in the discovery of cancers' molecular mechanisms have led to the emergence of **a large number of targeted therapies.**
- However, these therapies do not show the same efficacy in all patients.

→ Clinicians must now **choose, for each patient**, between several chemotherapies, immunotherapies and targeted therapies, **based on several type of criteria** (biomarkers, clinical data…)

Numerous clinical decision-support solutions have been developed in the last few years, but there is still a need for a complete tool to help analyze all these data and **choose the most appropriate treatment.**

- The global Clinical Decision Support Systems market is expected to reach **3 to 10$ Billions** by 2027 with a CAGR of **9,5%** until 2030.

Existing solutions

Today there are more and more solutions to help clinicians in the cancer treatments' choice

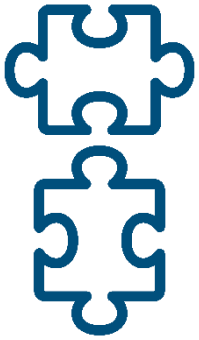
- Prognostic and Diagnostic tests: search for mutations, measurement of gene expression for specific genes involved in cancer mechanisms, etc.

Isolated biomarker analysis Companion diagnostic for 1 corresponding drug only	GOAL	Evaluate whether a given treatment can be administered to a patient
Multiple biomarker analysis In Vitro Diagnostic Multivariate Index Assays (IVDMIA)	GOAL	Identify presence and/or quantity of several biomarkers in a biopsy of a patient in order to select a treatment between different options

- More recently, e-solutions and AI based solutions reached the market to analyze all the available patient data
  - New players are offering complete solutions **incorporating multivariate diagnostic and artificial intelligence** to analyze the vast amount of data generated by all these tests.

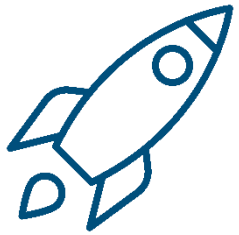
The innovation

Our solution : New complementary biomarker analysis technique



- Can be integrated in other diagnostic & e-Health solutions
- Provides more relevant data on the expression of genes of interest, thanks to **innovative standardization of measurements**
- Allows to identify **the most deregulated signaling pathway** and choose **the most** relevant treatment

- Our solution gives a **normalized expression score**, based on the comparison of the tumor sample to a data base of **specific comparative samples**
- This normalized expression score, or deregulation score, is more predictive of treatment response than the raw expression of genes



How does it work?

Analysis of tumor gene expression

Normalization of gene expression by comparison with a bank of healthy tissues and cells

The algorithm provides a **score** for each gene that reflects their **relative deregulations**

Core of the innovation:
normalization with gene expression level in
- the organ of the cancer (healthy + benign tumor)
and
- in normal cellular subtypes of this organ

RESULTS :

List of the genes RANKED from the most deregulated to the least deregulated

- Allows to identify **which molecular pathway is the most deregulated**
- Thus **which targeted treatment will be the most effective on this patient**

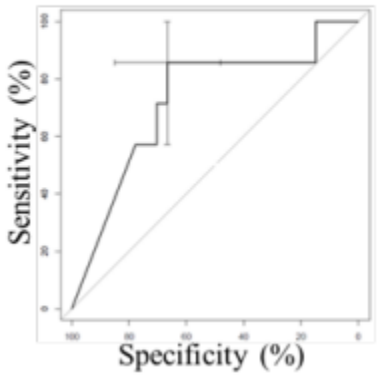
Proof of Concept: a better prediction ability

Prediction of sunitinib efficacy in a retrospective ccRCC clinical study

- We investigated the performance of PREDMED VEGFR2-scoring to predict the clinical effect of sunitinib for patients affected by clear cell renal-cell carcinoma (ccRCC)

VEGFR2-score and response to sunitinib

A



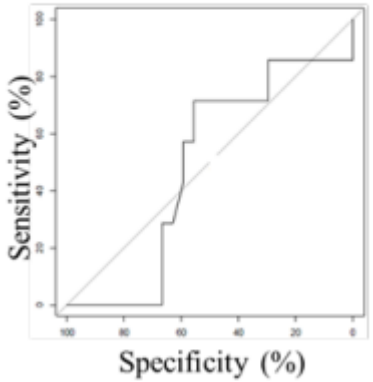
B

PR/CR	N = 6 Sensitivity 86%	N = 1
SD/PD	N = 9	N = 18 Specificity 67%
	VEGFR2-score > 637	VEGFR2-score < 637

AUC: 72.5% (50.1%-94.9%)
p = 0.04

VEGFR2 raw expression and response to sunitinib

C



D

PR/CR	N = 5 Sensitivity 71%	N = 2
SD/PD	N = 12	N = 15 Specificity 56%
	VEGFR2 expression > 0.79	VEGFR2 expression < 0.79

AUC: 48.4% (25.2%-71.6%)
p = 0.32 (ns)

PR/CR represents the number of partial and complete responses
SD/PD represents the number of stable and progressive diseases

- VEGFR2-PREDMED-score was more effective than raw VEGFR2-expression rate to relates with overall-response rate to sunitinib, progression-free survival and overall survival

Verlingue, L., Morel, D., Schaeffer, M., Tanguy, L., Schmidt, J., Bernhard, J., Loubaton, B., & Bagnard, D. (2021). Denoised VEGFR2 expression relates to sunitinib efficacy in advanced clear cell renal cell carcinoma. Biomed J Sci & Tech Res, doi: 10.26717/bjstr.2022.40.006529

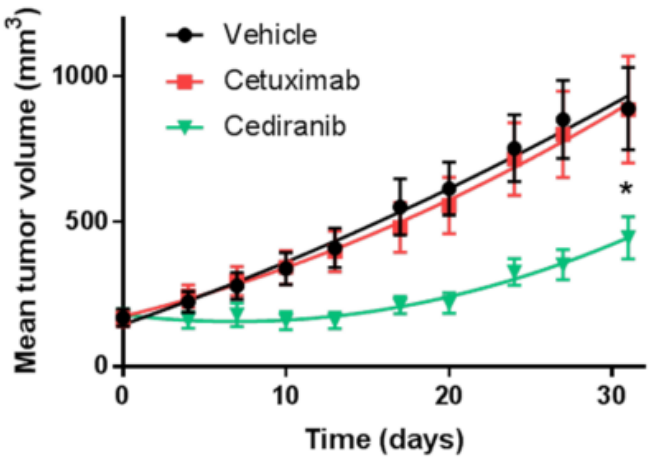
Proof of Concept: easier treatment identification

Prediction of drug efficacy in colon cancer PDX model

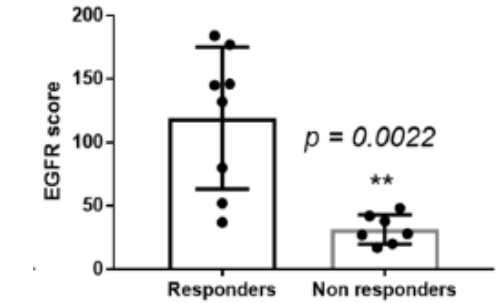
- A known cetuximab-resistant PDX model was assessed through PREDMED-score, 9 target genes were scored: the EGFR-score was very low, whereas the **PREDMED-test revealed a high deregulation of FLT1.**
- The two drugs were assessed in the corresponding PDX-model : as expected, Cetuximab (anti-EGFR) was inefficient, while Cediranib (anti-FLT1) treated mice showed a **significant 50% reduction of tumor growth** compared to Cetuxiamb and control groups.

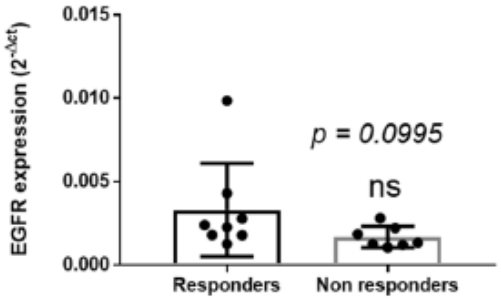
Evaluation of the predictive value of the scores in the PDX model: Ranking of target genes obtained after normalization of the expression data in PDX

Target genes	Score
FLT1	1000
KDR	575
VEGFA	437
MMP9	118
ERBB2	62
ITGB1	46
EGFR	28
PDGFRA	15
MMP2	0,01



Discrimination of Cetuximab responders versus non-responders





Fritz, J., Lefebvre, O., Fernandez, A., Schmidt, J., & Bagnard, D. (2020a). Prediction of Drug Efficacy in Colon Cancer Preclinical Models Using a Novel Ranking Method of Gene Expression. *Cancers*, *12*(1), 149. https://doi.org/10.3390/cancers12010149

Take the opportunity!

- Patented technology – WO2017/085326 published in May 2017 – EU, US, CA
- Can be integrated in diag or e-Health solutions already deployed
- Allows clinicians to identify, for each patient, the most relevant targets to be considered and to **select the most appropriate & efficient treatment** among the available targeted & immunotherapies
- Other uses as a companion test for clinical trials for a better patient selection

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