

RAIDs

Rational molecular
Assessment
Innovative Drug
selection

Translation

RAIDs1 to RAIDs 2

 **EORTC**
The future of cancer therapy

CHICAGO JUNE 1-2 2016
Suzy Scholl (Institut Curie)



A European Project supported through the Seventh Framework Programme for Research and Technological Development



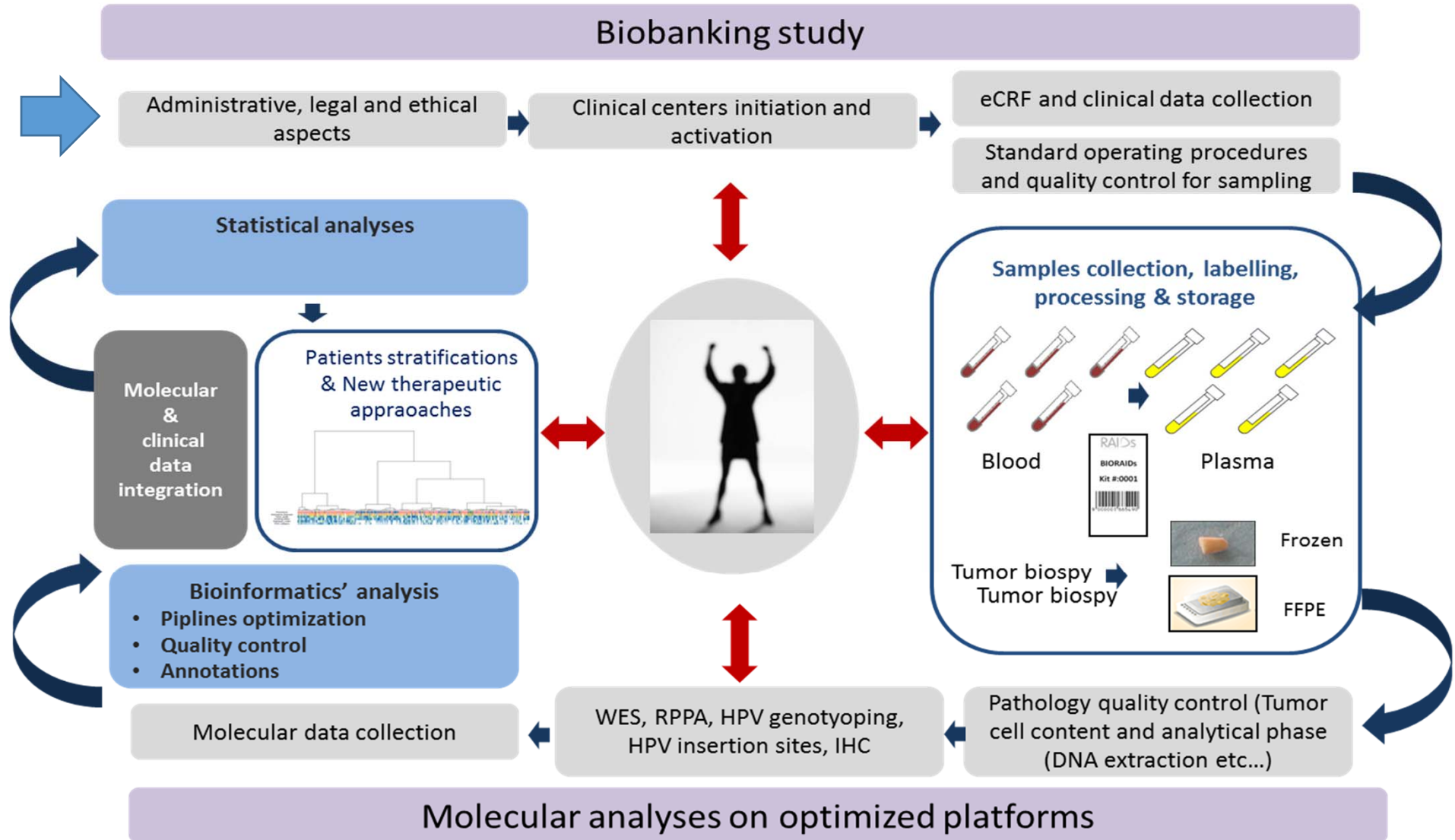
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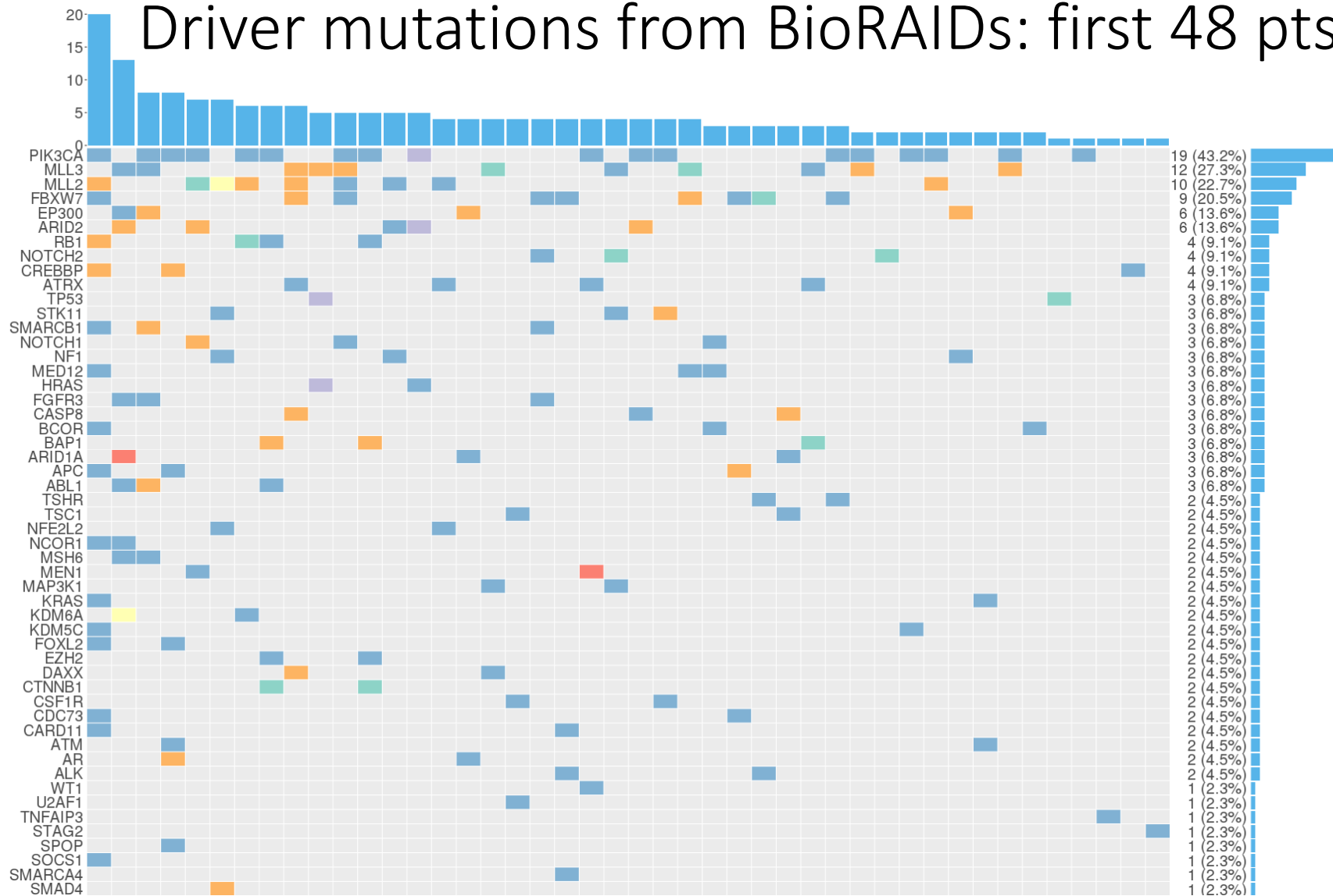
Clinical
Preclinical

BioRAIDs: longitudinal study at the heart of the RAIDs project





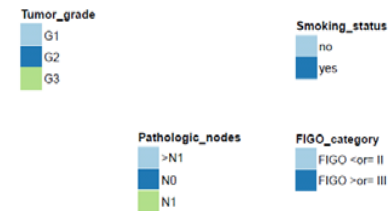
Driver mutations from BioRAIDs: first 48 pts



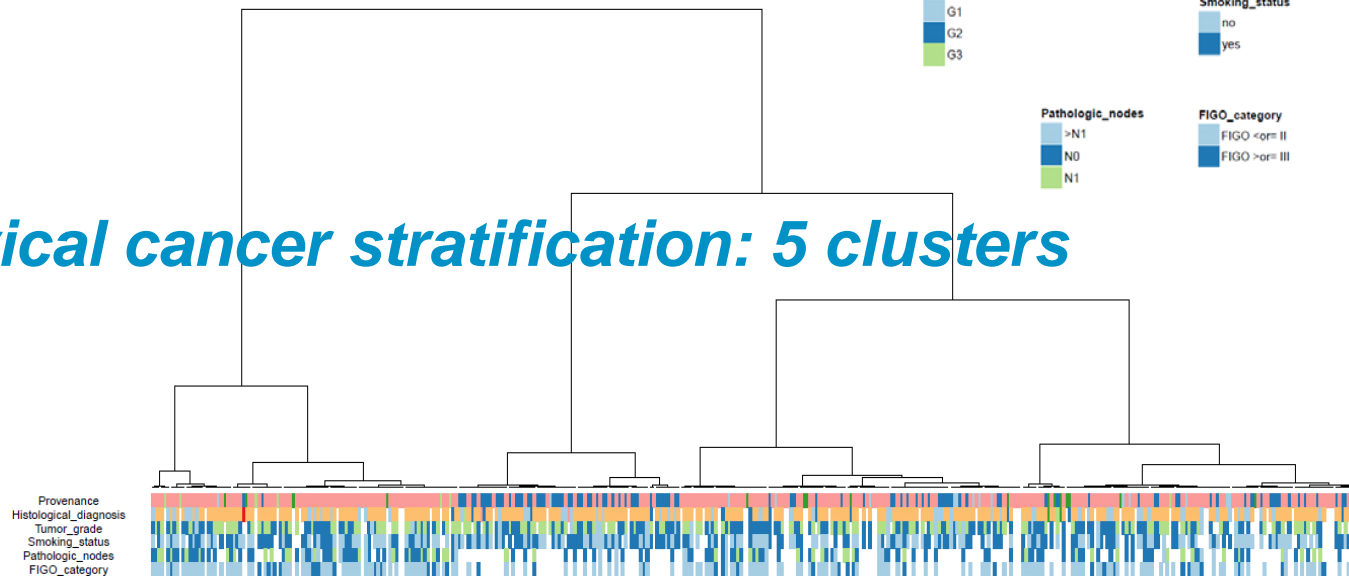


- Full exome sequencing: first analysis from 3 sets of data

- TCGA squamous cell carcinoma of cervix
- Helga Salvesen (Ojesina paper, Nature)
- RAIDS : full exoms from Tumors + 20 cell lines



Cervical cancer stratification: 5 clusters

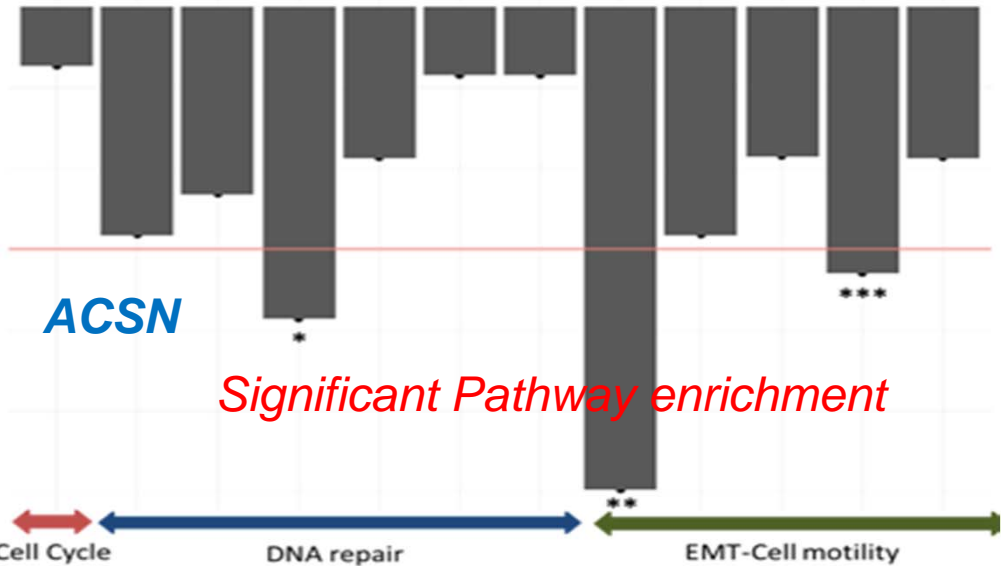


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*DNA repair-S phase checkpoint



**EMT-Cell motility-Cell matrix adhesion



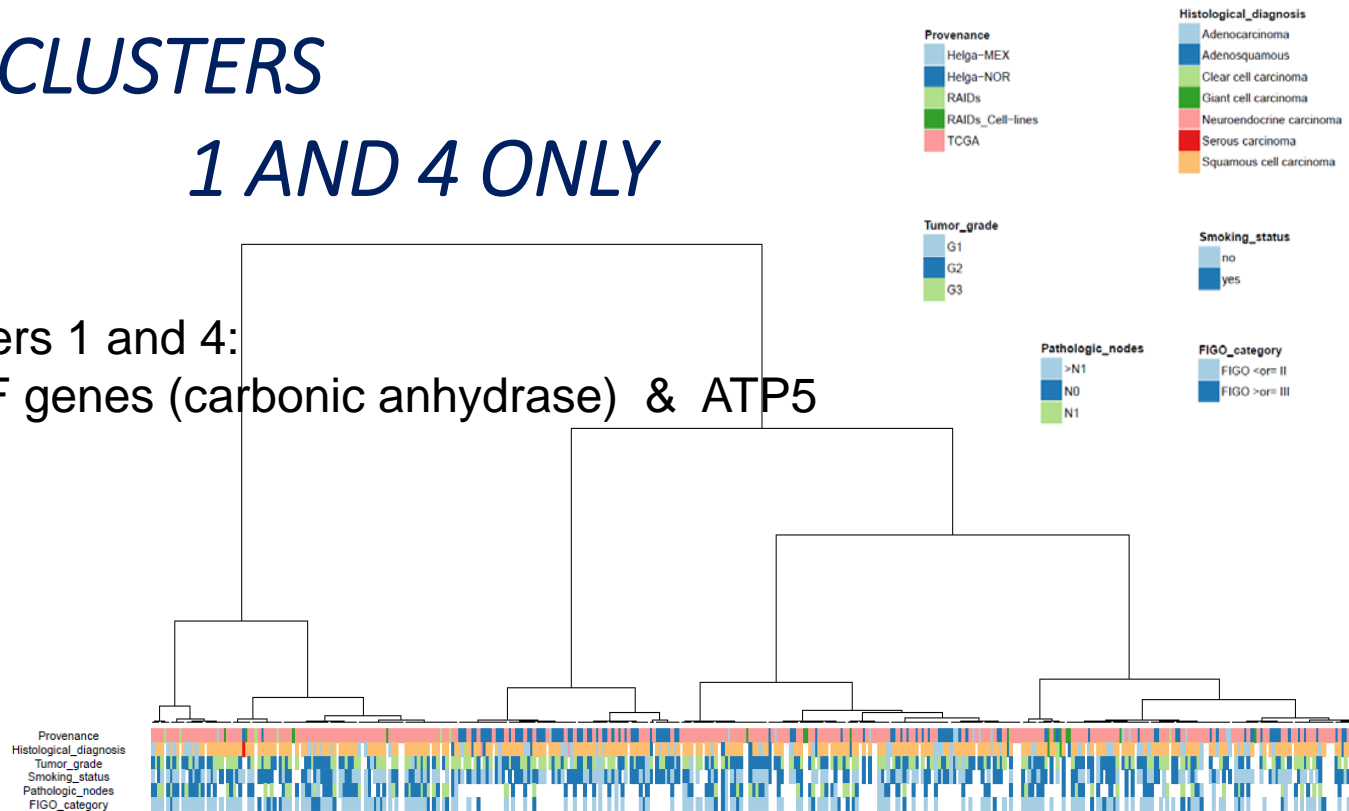
***EMT-Cell motility-ECM





CELL LINES IN CLUSTERS 1 AND 4 ONLY

Clusters 1 and 4:
NDUF genes (carbonic anhydrase) & ATP5

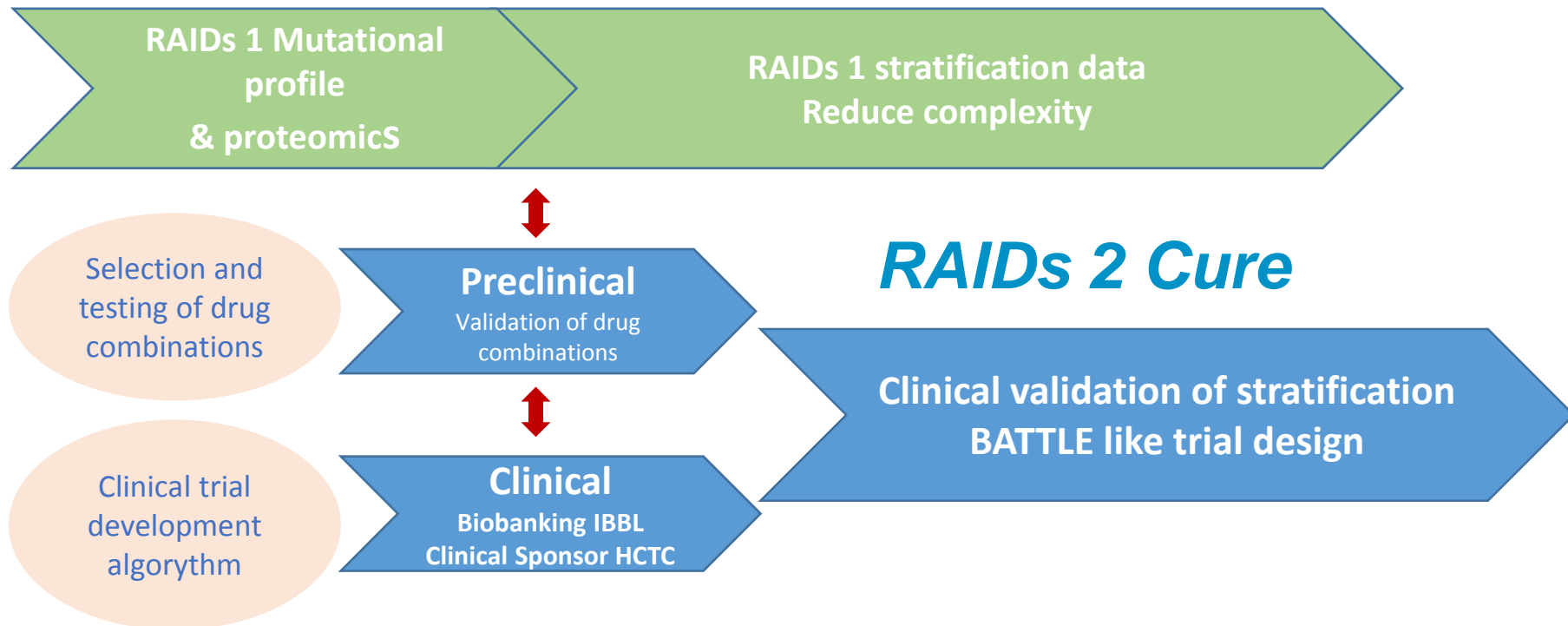


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RAIDs 1



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Precision Oncology: Lancet Oncology EDITORIAL Feb 2016

Imatinib (bcr/abl) Vemurafinib (Braf):

Basket studies show that same targeted therapy have not the same effect across tumour types

EFFICACY evaluation: it is the number of mutations that matter !!!!!

➤ IN NEED OF EMPIRICAL VALIDATION

Exceptional/super responders (MDA) are reported

- ❖ omissions in reporting the number of patients tested to find super response
- ❖ number of previous lines not a valid criteria (patients who respond 6-8X or better outcome –likely due to less mutations)
- ❖ few prospective trials reported: Shiva trial is the only prospective trial (Curie)
- ❖ TOXICITY not negligible

➤ BASED ON PRECISION DIAGNOSTICS

Detailed gene mutation / expression profiling needed

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Precision medicine remains unproven

& as such is

a hypothesis in need of vigorous testing

RAID^s

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Clinical

Preclinical: cell line work (20)



Drug testing in cell lines: Inserm Grenoble

| Molécule | cible | CRL1550 | CRL7920 | HeLaRPMI | HTB31 | HTB34 | HTB35 | CRL1594 | CRL1595 | CRL2614 | CRL10302 | HTB32 | HTB33 | IC1 | IC3 | IC4 | IC5 | HeLa | CSCC7 | CC11- | CC11+ | CC10B | CC10A | CSCC8 | C33A |
|---------------|---------------------|---------|---------|----------|-------|-------|-------|---------|---------|---------|----------|-------|-------|-----|-----|-----|-----|------|-------|-------|-------|-------|-------|-------|------|
| Vorinostat | HDAC | | | | | | | | | | | | | | | | | | | | | | | | |
| Tamoxifène | ER | | | | | | | | | | | | | | | | | | | | | | | | |
| Gefitinib | EGFR | | | | | | | | | | | | | | | | | | | | | | | | |
| Sunitinib | VEGFR... | | | | | | | | | | | | | | | | | | | | | | | | |
| Doxorubicine | intecalant | | | | | | | | | | | | | | | | | | | | | | | | |
| Erlotinib | topoisomerase | | | | | | | | | | | | | | | | | | | | | | | | |
| Lapatinib | EGFR | | | | | | | | | | | | | | | | | | | | | | | | |
| Gemcitabine | DNA replication | | | | | | | | | | | | | | | | | | | | | | | | |
| Irinotecan | Topoisomerase | | | | | | | | | | | | | | | | | | | | | | | | |
| L6 | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| Sorafinib | Raf/EGFR/DFGR/KIT | | | | | | | | | | | | | | | | | | | | | | | | |
| Crizotinib | ALK/ROS/MET | | | | | | | | | | | | | | | | | | | | | | | | |
| Dasatinib | BCR-abl... | | | | | | | | | | | | | | | | | | | | | | | | |
| Metformine | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| L3 | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| Paclitaxel | Tubiline | | | | | | | | | | | | | | | | | | | | | | | | |
| Phenformine | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| Vinblastine | Tubiline | | | | | | | | | | | | | | | | | | | | | | | | |
| 5-FU | thymidilate syntase | | | | | | | | | | | | | | | | | | | | | | | | |
| Melphalan | alkylant | | | | | | | | | | | | | | | | | | | | | | | | |
| Vinorelbine | Tubiline | | | | | | | | | | | | | | | | | | | | | | | | |
| STO609 | CamII kinase | | | | | | | | | | | | | | | | | | | | | | | | |
| T6 | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| Etoposide | TKI/KI | | | | | | | | | | | | | | | | | | | | | | | | |
| Colchicine | Tubiline | | | | | | | | | | | | | | | | | | | | | | | | |
| Topotecan | topoisomerase | | | | | | | | | | | | | | | | | | | | | | | | |
| Dauvorubicine | intercalant | | | | | | | | | | | | | | | | | | | | | | | | |
| Fasudil | ROCK | | | | | | | | | | | | | | | | | | | | | | | | |
| Imatinib | BCR-abl... | | | | | | | | | | | | | | | | | | | | | | | | |
| Dacarbazide | alkylant | | | | | | | | | | | | | | | | | | | | | | | | |
| cisplatine | DNA crosslinker | | | | | | | | | | | | | | | | | | | | | | | | |
| Cytarabine | | | | | | | | | | | | | | | | | | | | | | | | | |
| Iniparib | PARP | | | | | | | | | | | | | | | | | | | | | | | | |
| Methotrexate | DHFR | | | | | | | | | | | | | | | | | | | | | | | | |
| T4 | BCR-abl... | | | | | | | | | | | | | | | | | | | | | | | | |
| Carboplatine | DNA crosslinker | | | | | | | | | | | | | | | | | | | | | | | | |
| EMD1214063 | c-MET | | | | | | | | | | | | | | | | | | | | | | | | |
| L7 | mitochondrie/AMPK | | | | | | | | | | | | | | | | | | | | | | | | |
| Chlorambucil | alkylant | | | | | | | | | | | | | | | | | | | | | | | | |
| Liminib | LIMK | | | | | | | | | | | | | | | | | | | | | | | | |

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RAIDs 1 to RAIDs2

LCSB

Luxembourg Center for System

Biomedicine