

Molecular dissection of colorectal cancer in pre-clinical models identifies patterns of intra-tumour heterogeneity and biomarkers predicting sensitivity to EGFR inhibitors

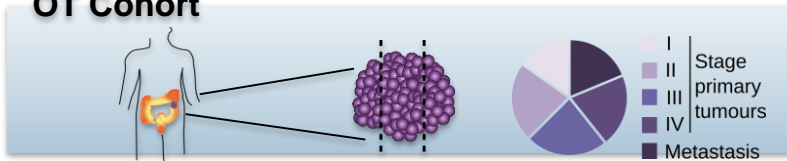
**Moritz Schütte, Alacris Theranostics GmbH,
On behalf of the OncoTrack consortium**

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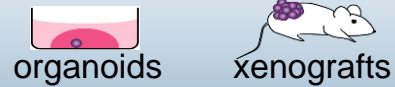
Methods for systematic next-generation oncology biomarker development



OT Cohort

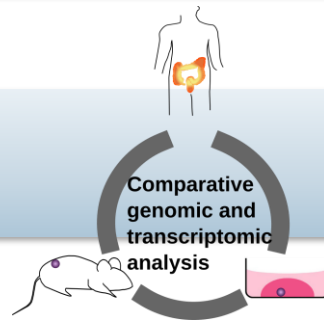


Preclinical models



Omics analysis

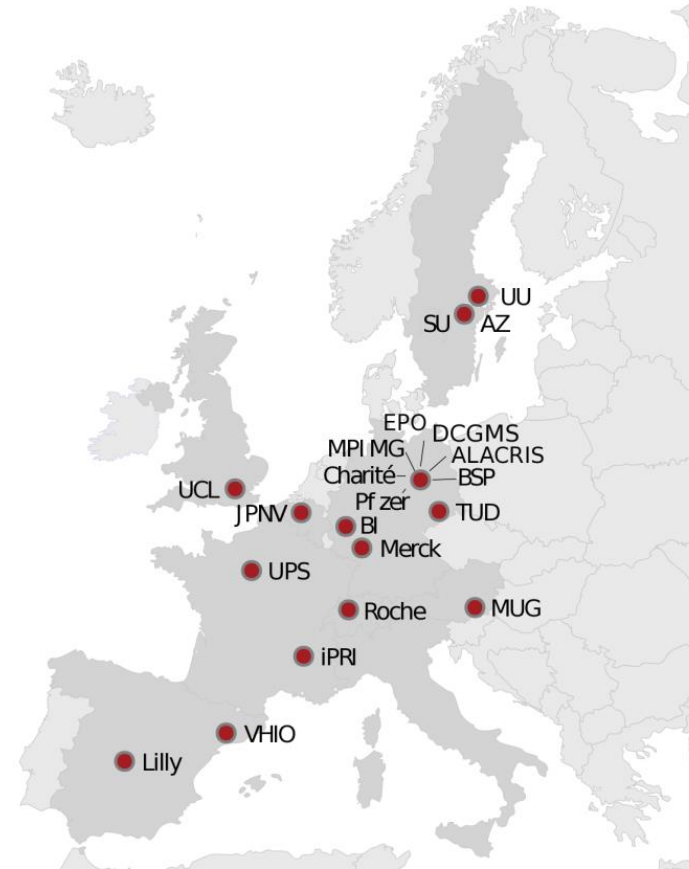
GenomeSeq
ExomeSeq
RNASeq
Methylome Array



Preclinical platforms

- EGFR blockade
- Chemotherapy
- MEK inhibitor
- mTOR inhibitor
- Angiogenesis inhibitors

Identification of biomarkers of drug sensitivity



Academia

EFPIA



UPPSALA
UNIVERSITET



SMEs



DCGMBS

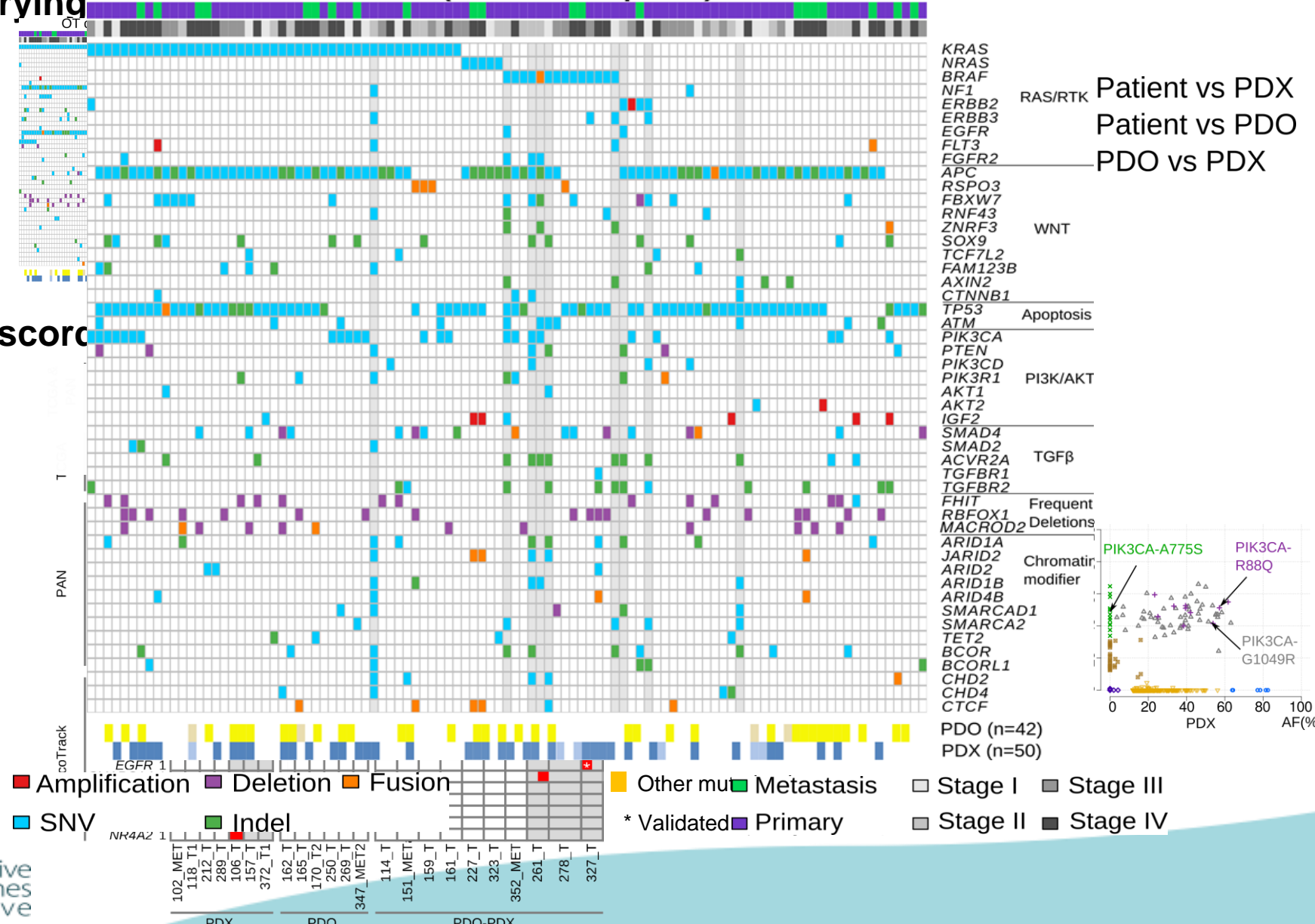


NGS analysis of matching patients, patient-derived xenografts (PDX) and organoids (PDO) gives insight into intra-tumour heterogeneity.

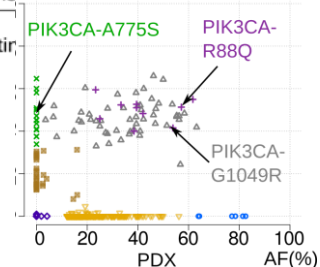
OT cohort (101 samples)

1) Varying

2) Discordant



Patient vs PDX
Patient vs PDO
PDO vs PDX

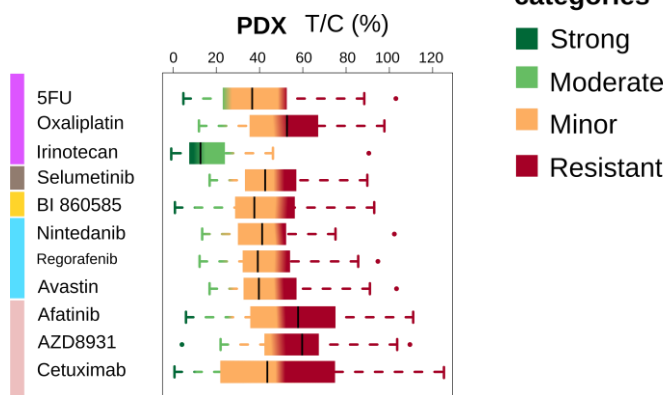
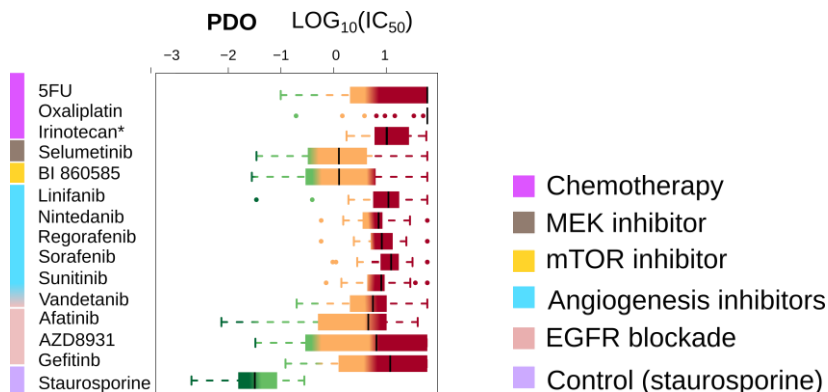


Drug screening using 16 compounds

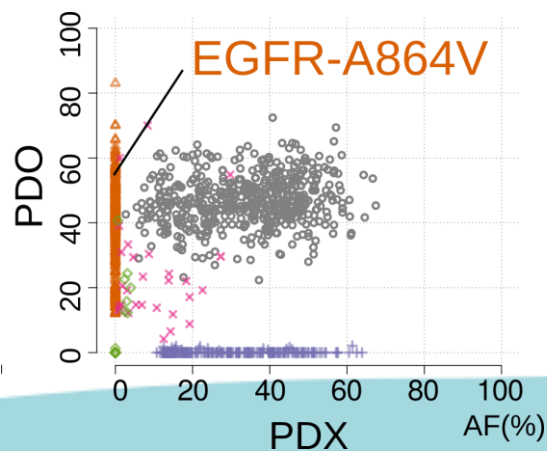
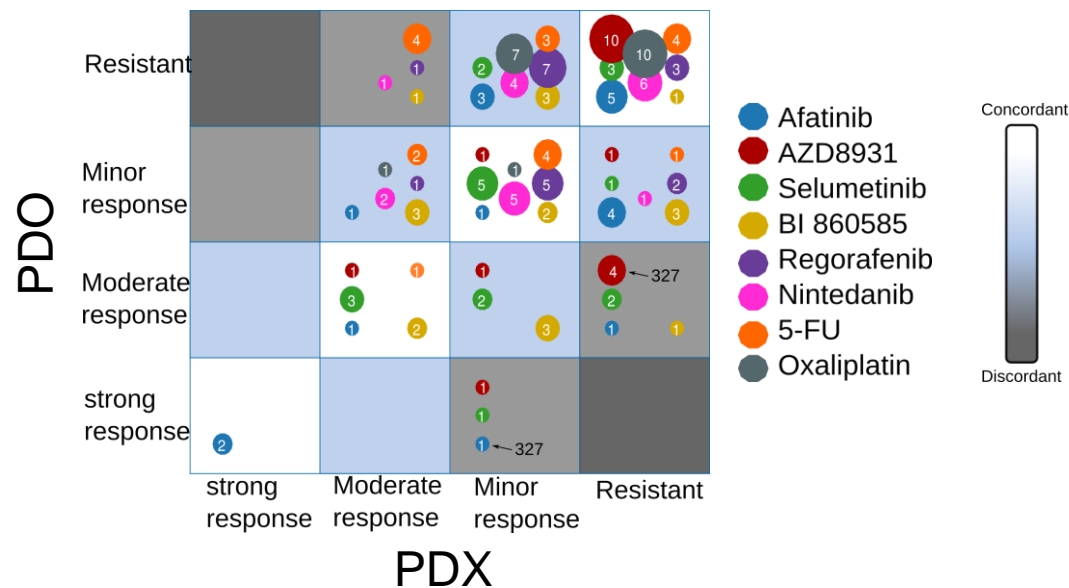
Drug sensitivity largely concordant between xenograft and organoid.

Interesting exceptions with potential implications on personalized medicine.

Drug Sensitivity

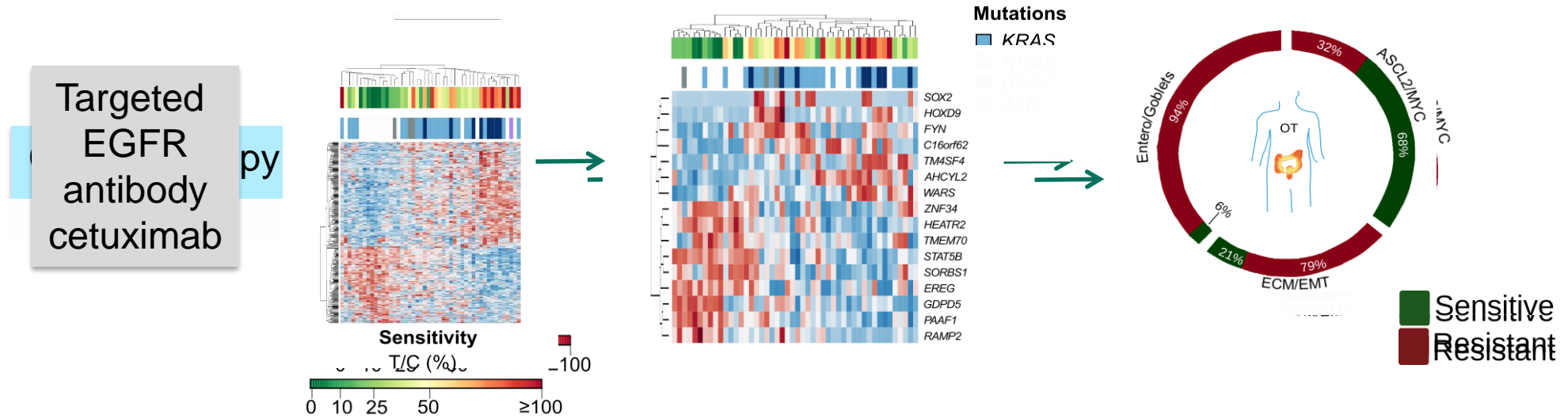


Drug sensitivity: PDX vs PDO



Interesting case for precision medicine:
 PDO-private EGFR mutation triggers drug response

New predictive gene expression signatures by combining molecular and drug sensitivity data



Cetuximab: Validation on external cohort

Mutation status in KRAS/BRAF/NRAS
Mutations status in KRAS codon 12/13
OT mini classifier

OT mini classifier
OT mini classifier

cases with mutation information (n=96)
cases with mutation information (n=155)
whole cohort (n=164)

WT KRAS codon 12/13 (n=96)
WT KRAS/BRAF/NRAS mutations (n=36)

