# Osmanbeyoglu Lab:
# From integrative modeling to biological and therapeutic insights

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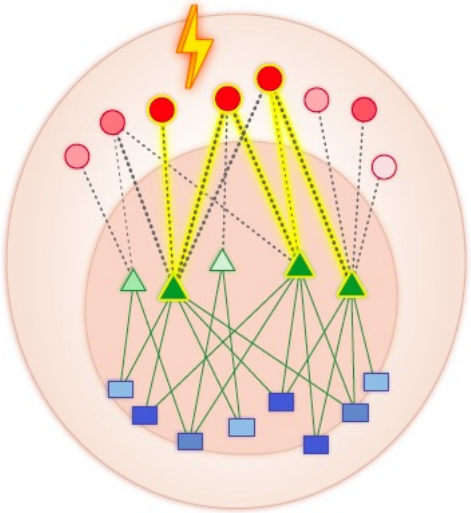
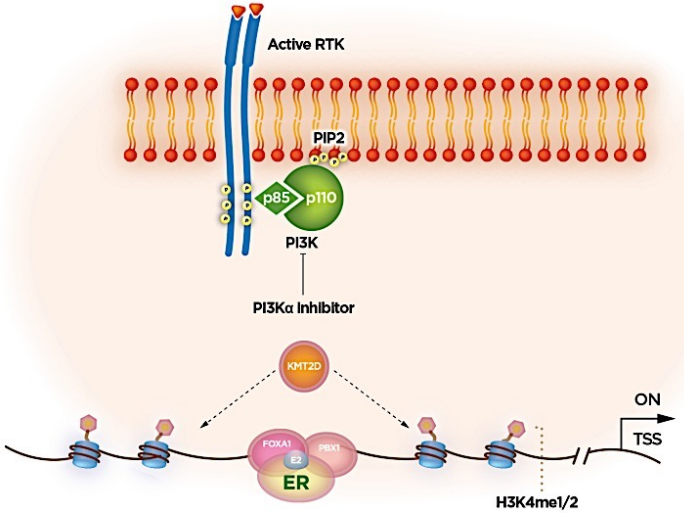
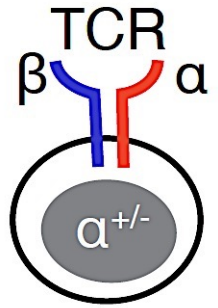
## Areas of Research



Systems biology




Epigenetics




Omics approaches in immunology

# Computational methods for delineating cell context-specific regulatory programs

**The ICI Fund (Innovation in Cancer Informatics), Role: PI (completed)**
**NIH/NIGMS R35 GM146989 — Role: PI**

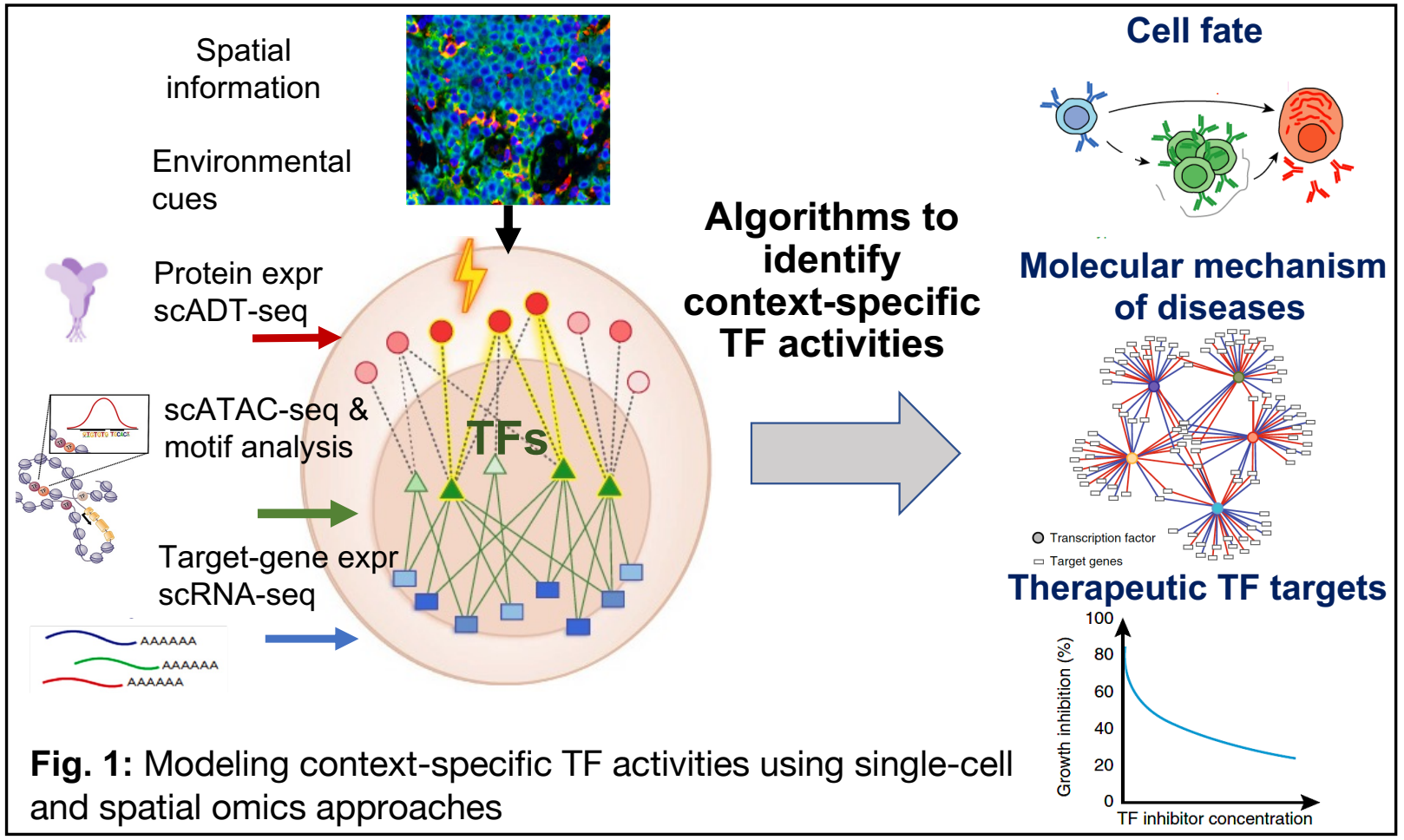



**Fig. 1:** Modeling context-specific TF activities using single-cell and spatial omics approaches

- **SPaRTAN** (Single cell Proteomic and RNA based Transcription factor Activity Network), a computational framework for linking cell-surface receptors to transcriptional regulators. (Ma et al, *Nucleic Acid Research*, 2021)

- **STAN** (Spatially informed Transcription Factor Activity Network), a novel computational method to predict spot-specific TF activities by utilizing spatial transcriptomics datasets and cis-regulatory information (Sagan et al, unpublished)

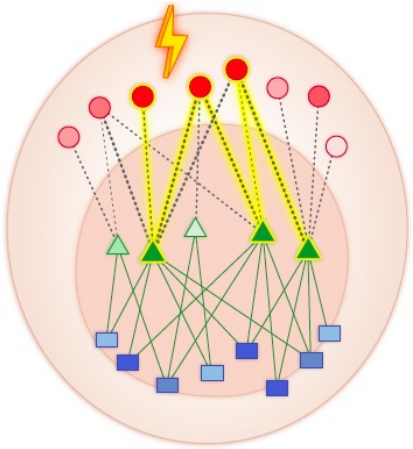
# Algorithms linking signaling pathways with transcriptional programs for precision medicine (1)

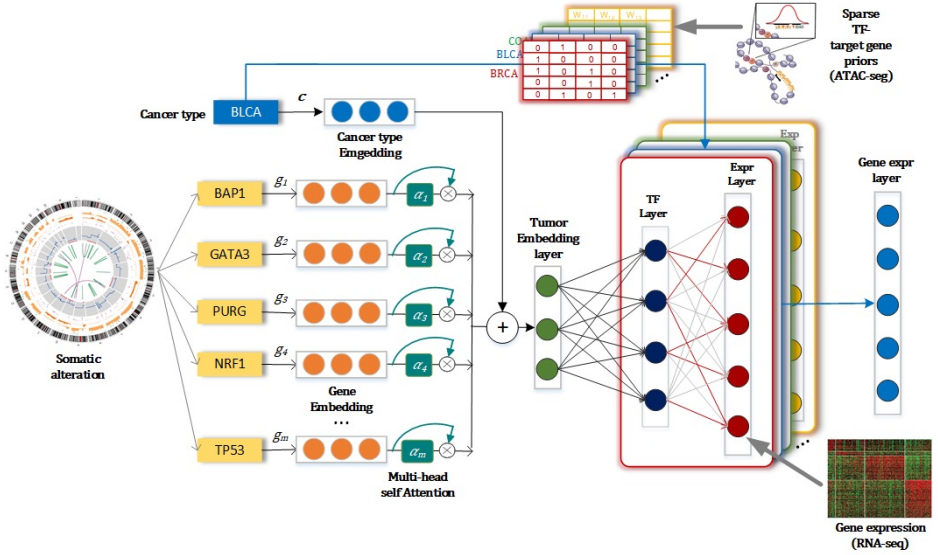
**NIH R00, Role: PI.**
**Grant Number: R00CA207871**

**Signaling proteins**

**Transcription factors**

**Target genes**






- Statistical approach for exploiting parallel multi-omics data to link dysregulation of upstream signaling pathways with altered transcriptional responses (Osmanbeyoglu et al., *Genome Research,* 2014)

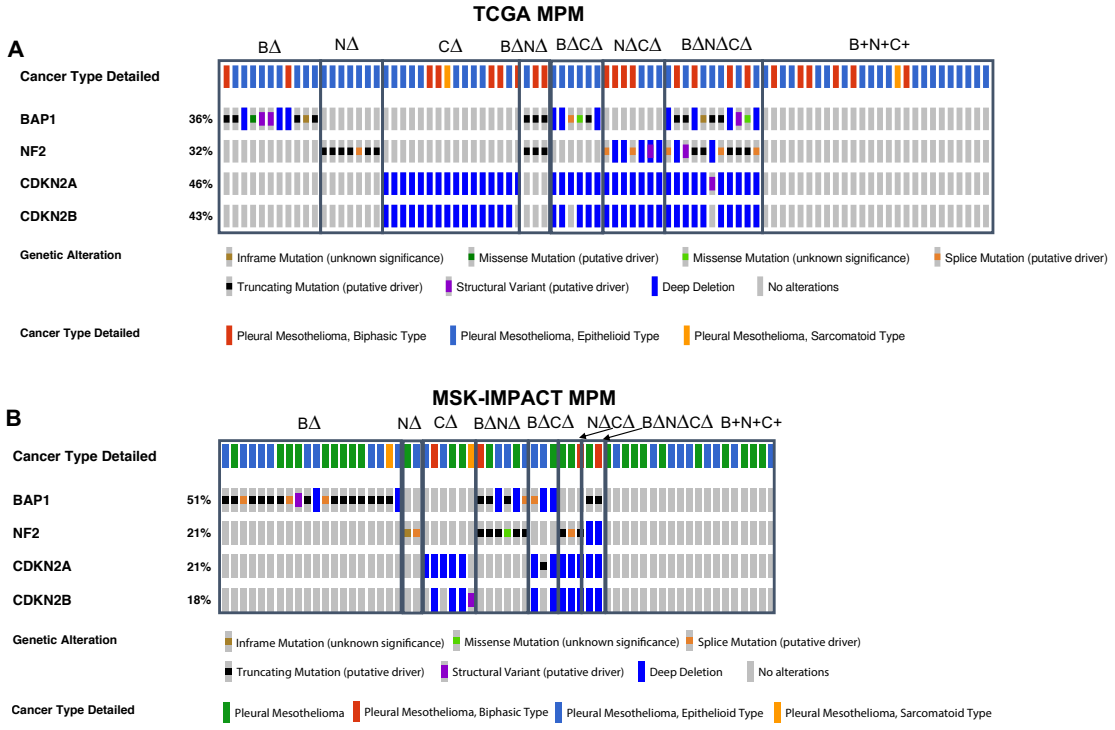
- Pan-cancer analysis identified impact of mutations on TF and (phospho)protein activities (Osmanbeyoglu et al., *Nature Communications*, 2017*)*

- **PSIONIC** (patient-specific inference of networks incorporating chromatin), a multi-task regression framework to predict patient-specific gene expression profiles from transcription factor (TF) binding motifs in chromatin-accessible elements. (Osmanbeyoglu# et al., *Nature Communications*, 2019*)* (#=co-corresponding authors)

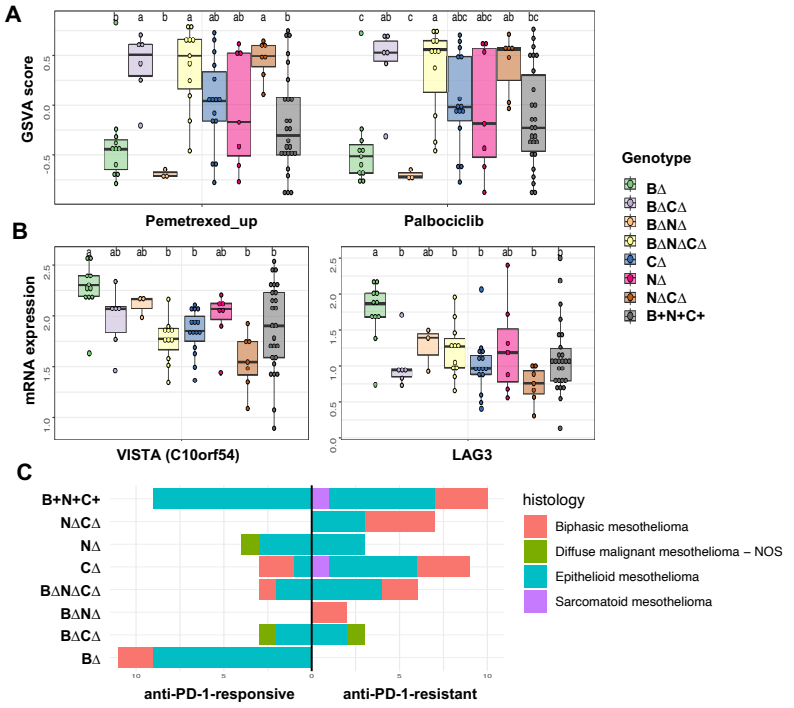
- **CITRUS (C**hromatin-informed **I**nference of **T**ranscriptional **R**egulators **U**sing **S**elf-attention mechanism), a partially interpretable neural network (NN) model with encoder-decoder architecture to link somatic alterations to transcriptional programs (Tao*, Ma* et al., *Nucleic Acids Research*, 2022) (corresponding author)

# Algorithms linking signaling pathways with transcriptional programs for precision medicine (2)

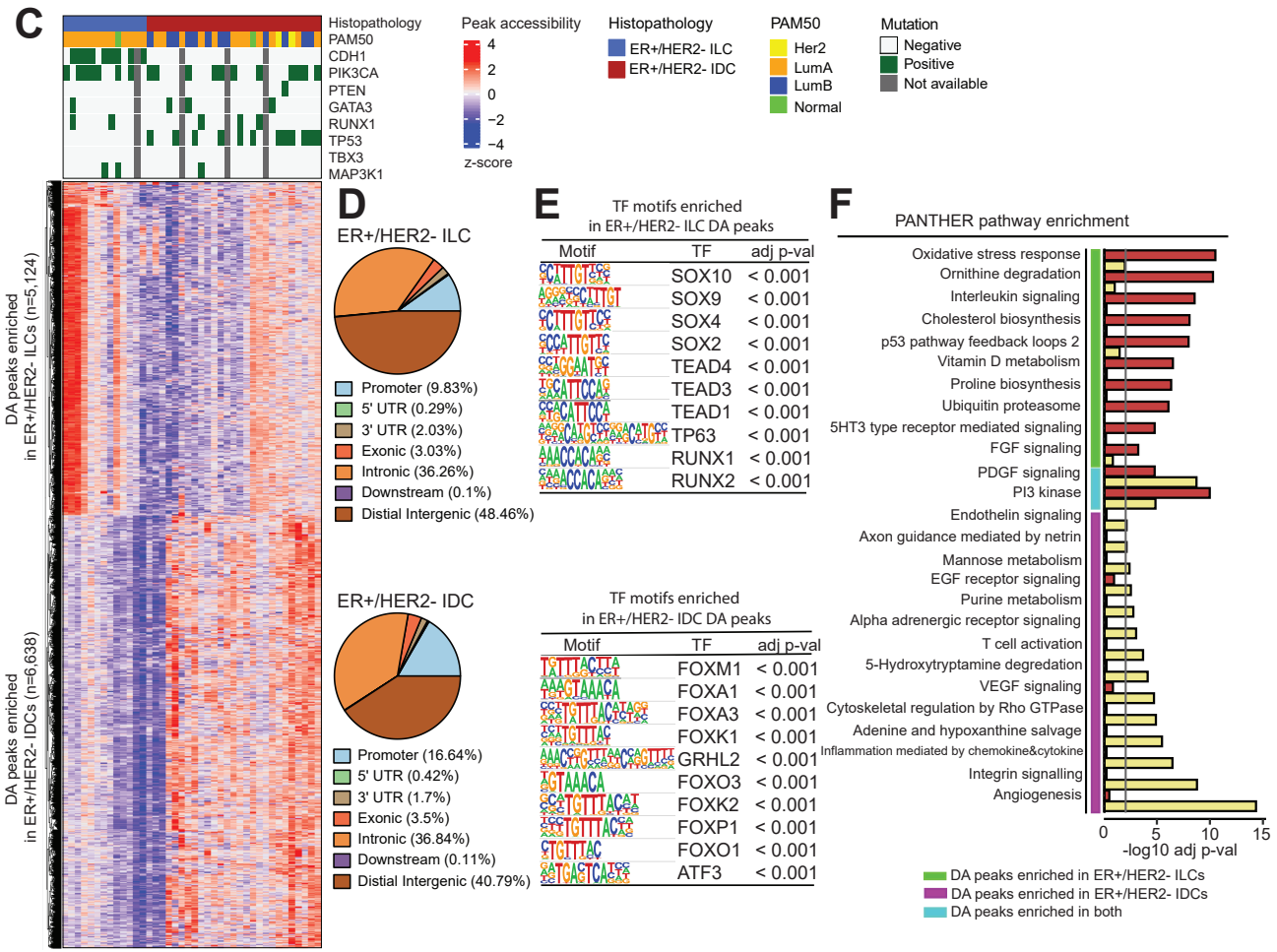
## NIH R00, Role: PI.
## Grant Number: R00CA207871



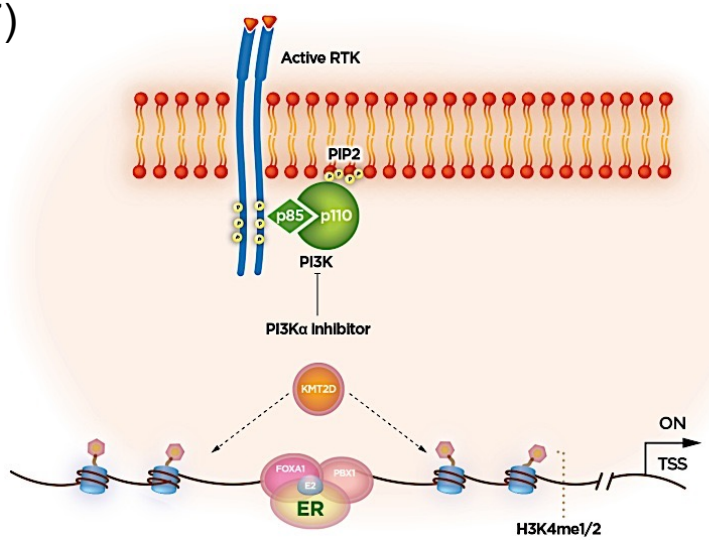

- Modeling impact of BAP1 mutation on transcriptional programs in malignant pleural mesothelioma (*Hmeljak et al., Cancer Discovery,* 2018)
- Isolated BAP1 loss in malignant pleural mesothelioma predicts immunogenicity with implications for immunotherapeutic response (Osmanbeyoglu et al., *Cancers,* 2022) (corresponding author)



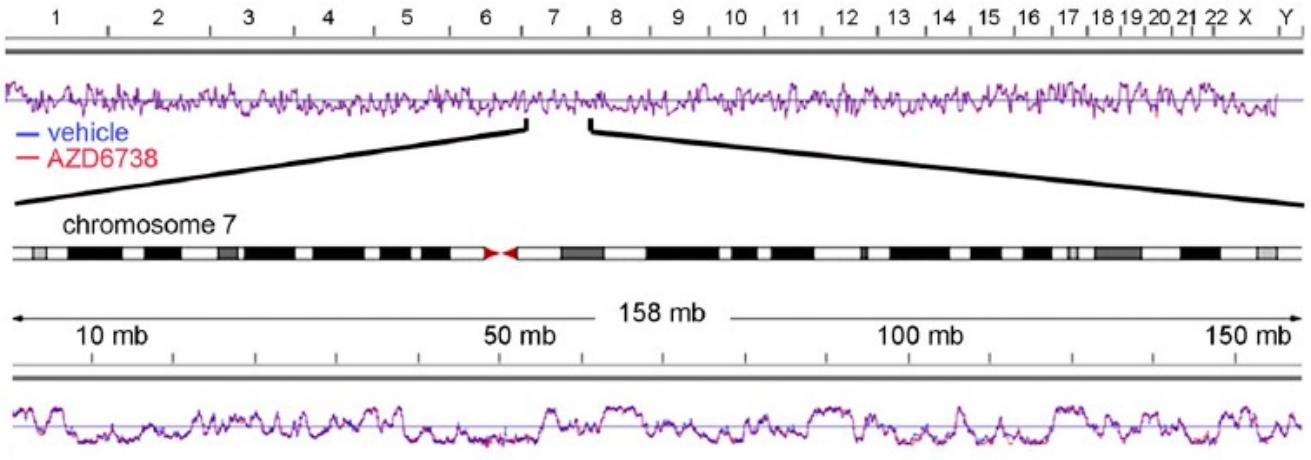
# Epigenetics and drug response

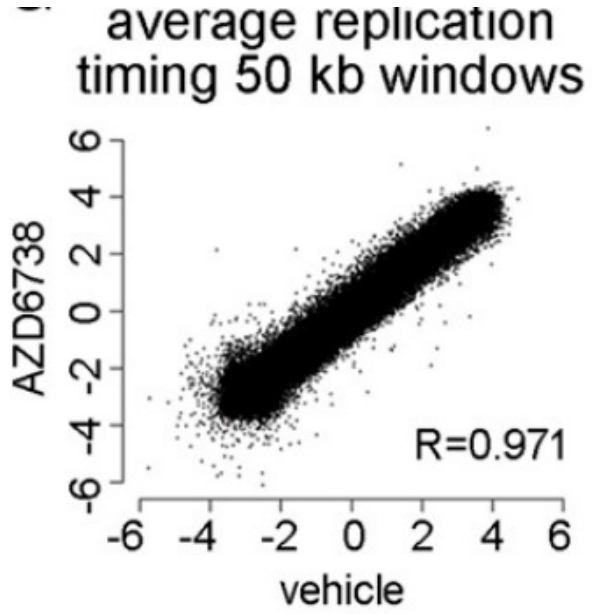



- Chromatin accessibility landscape and active transcription factors in primary human invasive lobular and ductal breast carcinomas (Lee, Osmanbeyoglu, *Breast Cancer Research*, 2022)
- Integrative multi-omics analysis to understand estrogen receptor (ER) mediated transcription (Osmanbeyoglu et al., *BMC Genomics*, 2012; Osmanbeyoglu et al., *NAR*, 2013; Watters et al., *Mol. Cell. Endocrinol, 2017)*
- Integrative multi-omics analysis to characterize the epigenomic and transcriptomic landscape of ER+ breast cancer models in response to the inhibitor of PI3K signaling (Toska, Osmanbeyoglu et al., *Science*, 2017)



# DNA replication and drug response

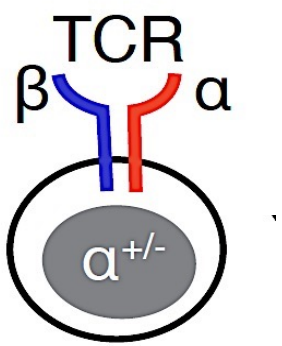


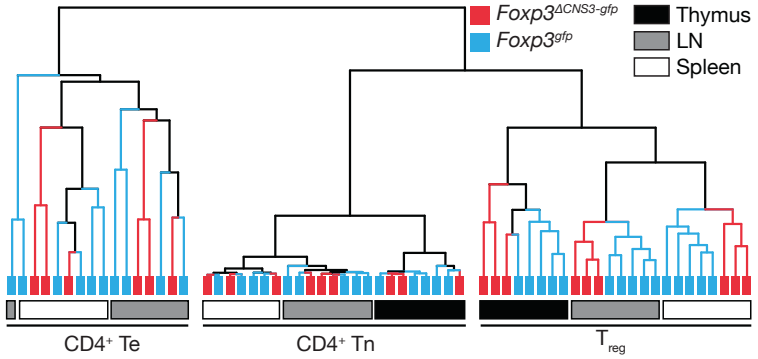




How targeted drugs induce changes in the timing of the replication program?

- WEE1 kinase inhibitor AZD1775 induces CDK1 kinase-dependent origin firing in unperturbed G1 and S phase cells (Moiseeva et al., *PNAS*, 2019)
- An ATR and CHK1 kinase signaling mechanism that limits origin firing during unperturbed DNA replication (Moiseeva et al., *PNAS*, 2019)
- Thymidine rescues ATR kinase inhibitor-induced deoxyuridine contamination in genomic DNA, cell death, and interferon-alpha/beta expression (Sugitani et al., Cell Reports, 2022)

# Omics approaches in immunology and immunotherapy




- Immune landscape in estrogen receptor positive breast cancer reveals divergent macrophage-driven microenvironment (Oskar et al, *Nature Cancer, In press*)
- Blocking of CA-MSC-induced desmoplasia reprograms the tumor immune microenvironment and enhances the efficacy of PD-L1 therapy (Casio et al., *Science Advances* , 2021)
- The role of Ets family TFs in T cell homeostasis (Luo, Osmanbeyoglu et al., *Nature Communications*, 2017)
- The genetic control of regulatory T cell development, in particular its selection of the TCR repertoire (Feng et al., *Nature*, 2015)