Gene expression in ROS1+ patient derived cell lines upon TKI treatment.

Lung cancer is the most common type of cancer worldwide and has the highest mortality rate. Approximately 1-2% of all lung cancers is ROS1 positive (ROS1+). Due to a translocation, ROS1 fuses with a partner and is thereby constitutively activated, which can result in oncogenesis. ROS1 has several known fusion partners, of which CD74, EZR and SDC4 are most frequently occurring. ROS1+ lung cancer is treated effectively with tyrosine kinase inhibitors (TKIs), that inhibit the activation of ROS1+. However, TKI treatment is not curable and most patients eventually develop resistance towards TKI treatment. TKI resistance can be on-target, e.g. point mutations that reduce the affinity for the TKIs, or off-target, e.g. bypass mechanisms and factors are activated inducing further oncogenesis. The exact mechanisms of ROS1+ TKI resistance, however, are not yet unravelled.

Here at the Hanze we are investigating these resistance mechanisms in patient derived ROS1+ lung cancer cells. To get a deeper understanding of these resistance mechanisms and factors in the patient, we want to perform omics studies on these patient derived cell lines. Omics studies explore the totality of specific factors, for example with proteomics all the proteins are examined and with trancriptomics all RNA. To study the transcriptomics in cells, RNA sequencing assays can be performed.

Interestingly, others have performed RNA sequencing on a panel of ROS1+ lung cancer patient derived cell lines, which we also have available for our research here, treated with ROS1+ specific TKIs: crizotinib or entrectinib (Peters et al. 2023, Chen et al. 2024). These RNA sequence datasets are publicly available at the Gene Expression Omnibus (GEO; [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE239844](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fgeo%2Fquery%2Facc.cgi%3Facc%3DGSE239844&data=05%7C02%7Cm.de.looff%40pl.hanze.nl%7C0527c2256fd34823a5cb08dd572893b6%7Ca3b390147adc48faa11437c2434dbd69%7C0%7C0%7C638762553958698572%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C0%7C%7C%7C&sdata=Hbg4TA7JlNsojZpcrkSdQx9hGMDKOygJ4SuxGeHnO8Q%3D&reserved=0) and <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE214715>). In this study, we want to perform an whole transcriptomic data-analysis to investigate increased or decreased RNA expression in patient derived cell lines upon TKI treatment.