Drug development done better with tissue-specific molecular pharmacology

In collaboration with our partners we can enhance the readout of *in vivo* / *ex vivo* pharmacology study by evaluating the drug candidate mode of action at a cellular level, by providing molecular pharmacology data in various tissue compartments and by identification/validation of molecular targets. Relevant results are obtained in a timely and cost-effective manner.

Cell behaviour in health and disease is intricately linked to the microenvironment of cells. Studying in vivo cell dysfunction and responses to drugs is what matters, but the interpretation of whole tissue analysis is often hampered by the complexity of the tissue.

Our approach assigns drug effects and cell behaviour in complex tissue to certain cell types. This compartmentalization will provide a better insight in the true pharmacological behaviour of your new compound in relation to the disease status.

We developed a well validated protocol for analysing gene expression profiles in subsets of cells in complex tissues from animal and human origin. Using laser dissection microscopy, we isolate predestined cells from tissue sections and subject their RNA to quantitative RT-PCR analysis. It provides a unique way to unmask the molecular control of cell behaviour in different compartments of healthy and diseased tissues. Also, the effects of therapeutic intervention can be analysed at the molecular level in the cells you are interested in.
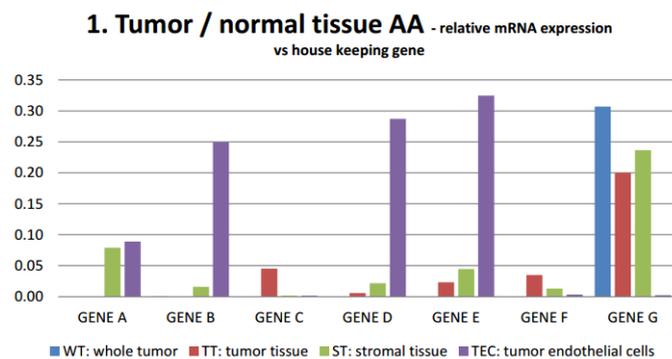
Experiment summary example

Study setup

A gene essential for the efficacy of your drug candidate has been identified. The efficacy study can be designed to monitor the expression levels in predestined cells or tissue compartments, both during and at the study end-point.

Results

The table below shows the expression levels in different compartments of the tumor and surrounding healthy tissue, and endothelial tumor cell line.

1. Tumor / normal tissue AA - relative mRNA expression vs house keeping gene

■ WT: whole tumor ■ TT: tumor tissue ■ ST: stromal tissue ■ TEC: tumor endothelial cells

Samples

The analysis can be performed on various samples, e.g. tumor sections, whole tumors &biopsies.

Conclusion

1. Laser microdissection was successful, resulted in successful enrichment of analysed genes.

2. The gene D and E are highly enriched in the tumor blood vessel compartment, comparable to the gene B which is considered to be a pan-endothelial marker gene.

3. The gene F and gene G are not enriched in the tumor blood vessel compartment.

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