

Tissue Models for Target Validation and Drug Testing

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Description of the scientific aims

We generate complex microtissues *in vitro* that faithfully recapitulate the histology of clinical cancer biopsies. Matching high content assays then aim to test and measure the effects of gene silencing or chemotherapeutic compounds on cancer cell lines, tissues or primary cells. Our miniaturized platform can test large numbers of investigational compounds in high content screening assays. In parallel, using primary cell cultures established from patient biopsies, we develop reliable chemosensitivity tests for applications for personalized medicine and target validation. This should allow better prediction of chemotherapy outcome in clinical settings (prognostics), explore possible drug synergies, drug resistance, or avoid patient over-treatment.

Selected publications 2010-

1. Åkerfelt M, Bayramoglu N, Robinson S, Toriseva M, Schukov HP, Härmä V, Virtanen J, Sormunen R, Kaakinen M, Kannala J, Eklund L, Heikkilä J, Nees M.: Automated tracking of tumor-stroma morphology in microtissues identifies functional targets within the tumor microenvironment for therapeutic intervention. *Oncotarget*. Oct 6;6(30):30035-56, 2015
2. Björk JK, Åkerfelt M, Joutsen J, Puustinen MC, Cheng F, Sistonen L, Nees M: Heat-shock factor 2 is a suppressor of prostate cancer invasion. *Oncogene* Jun 29, 2015.
3. Björkman M, Östling P, Härmä V, Virtanen J, Mpindi JP, Rantala J, Mirtti T, Vesterinen T, Lundin M, Sankila A, Rannikko A, Kaivanto E, Kohonen P, Kallioniemi O, Nees M: Systematic knockdown of epigenetic enzymes identifies a novel histone demethylase PHF8 overexpressed in prostate cancer with an impact on cell proliferation, migration and invasion. *Oncogene*. Jul 19;31(29):3444-56, 2012.
4. Härmä V, Knuutila M, Virtanen J, Mirtti T, Kohonen P, Kovanen P, Happonen A, Kaewphan S, Ahonen I, Kallioniemi O, Grafström R, Lötjönen J, Nees M: Lysophosphatidic acid and sphingosine-1-phosphate promote morphogenesis and block invasion of prostate cancer cells in three-dimensional organotypic models. *Oncogene* Apr 19;31(16):2075-89, 2012.
5. Härmä V, Virtanen J, Mäkelä R, Happonen A, Mpindi JP, Knuutila M, Kohonen P, Lötjönen J, Kallioniemi O, Nees M: A comprehensive panel of three-dimensional models for studies of prostate cancer growth, invasion and drug responses. *PLoS One*. May 3;5(5):e10431. doi: 10.1371, 2010.