NoSarC.no, – Norwegian Sarcoma Consortium.

A national, prospective and population-based study of mutations and mechanisms in sarcomas, and preclinical validation of novel targeted therapies, with the intention to lead to clinical trials

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Norwegian Health Service

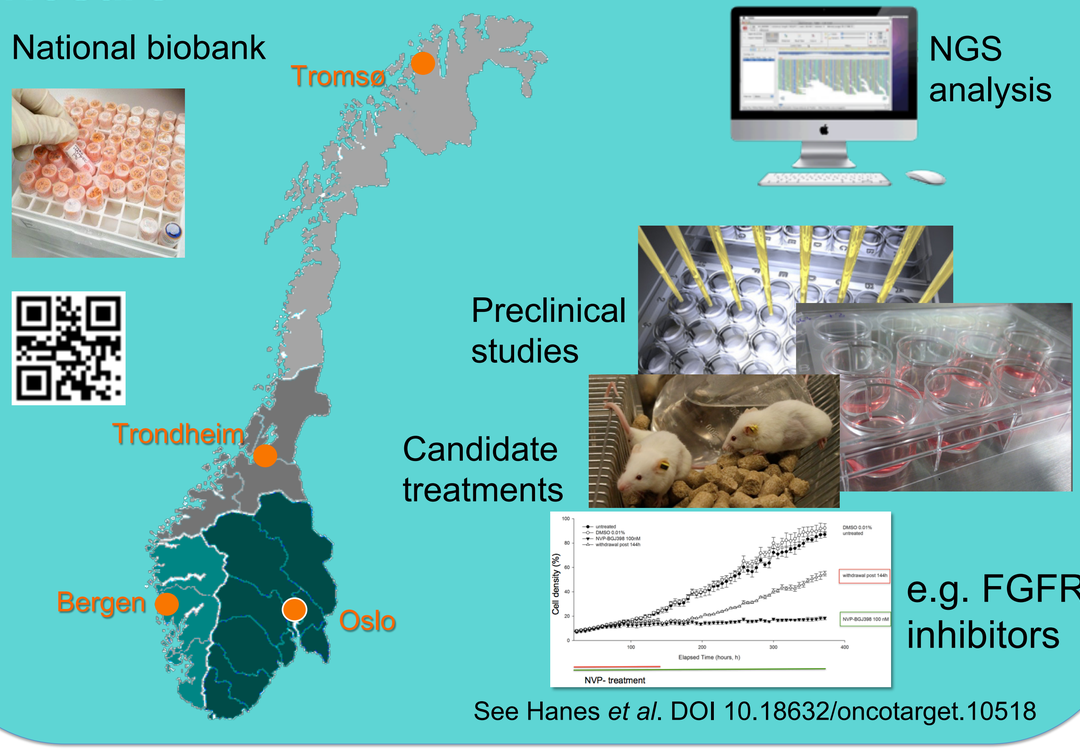
The Norwegian Sarcoma Consortium, NoSarC, is a collaborative research project involving all Norwegian Sarcoma Clinics.
Objectives are:

- to better understand sarcoma biology
- to identify biomarkers indicating sensitivity to therapies already developed and approved for treatment of more common cancers
- to validate candidate therapies in preclinical sarcoma models
- to provide evidence supporting clinical use

To achieve this, we

- prospectively collect samples from “all” Norwegian sarcoma patients over several years
- identify mutations by exome sequencing
- perform preclinical target evaluation in derived cell line and pdx models, as well as older non-matched models

NoSarC



See Hanes *et al*. DOI 10.18632/oncotarget.10518

Secondary objectives

- Establish xenografts and in vitro cell lines from patient material, with the advantage of knowing their somatic mutations
- Investigate effects of germ-line variation by analysing blood samples, including those from participants without tumour samples and a large collection of older patient blood samples

See Ballinger et al. Lancet Oncol DOI 10.1016/S1470-2045(16)30147-4

- Investigate the opinions of our patients by our ELSA group

Added value from national collaboration

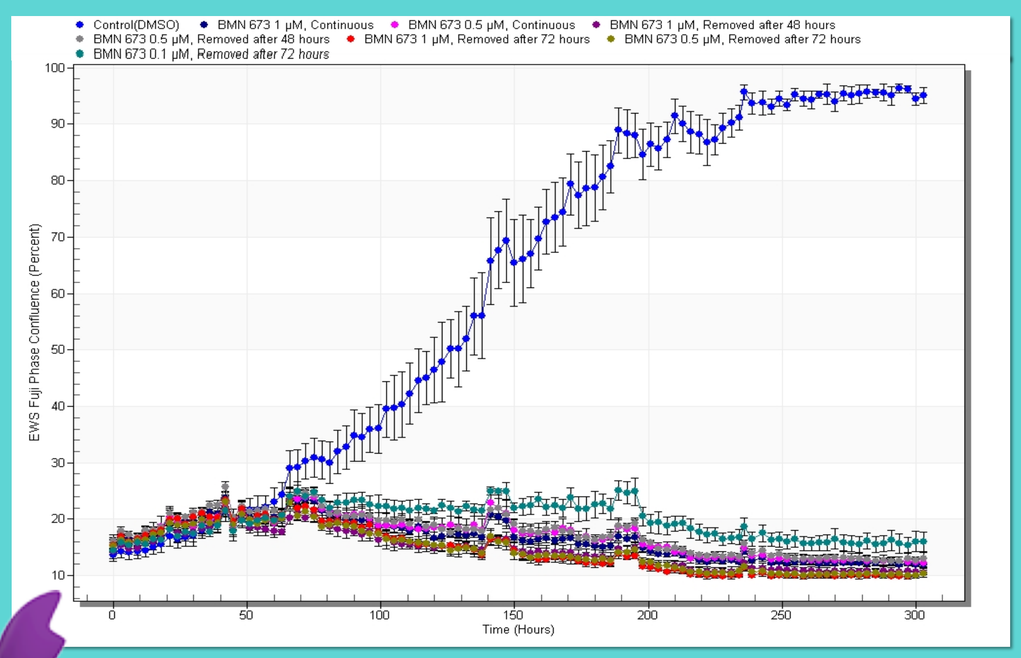
- Population-based data
- National evaluation of mutation frequencies and health-economic consequences
- Standardized genomic analysis

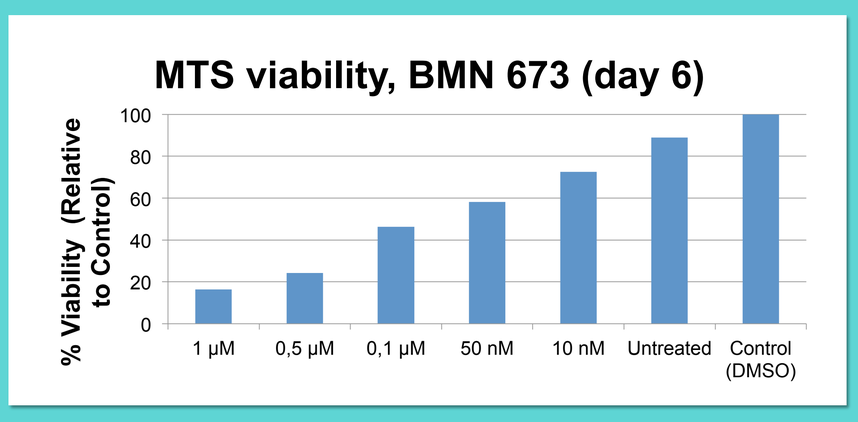
Germ-line data feed into national variant database, see 1000genomes.no

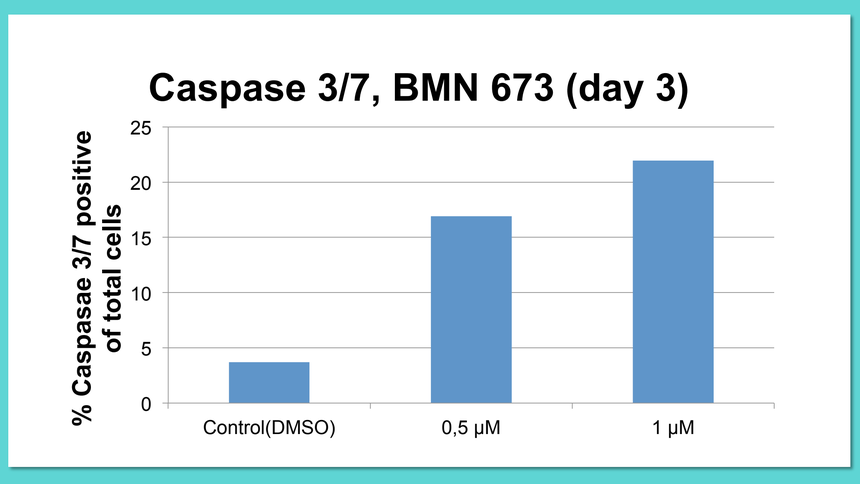
Preclinical testing *in vitro* - PARP-inhibitor BMN 673 has therapeutic potential in selected osteosarcoma cells

Many osteosarcomas (OS) have BRCA-like mutation profiles (Engert et al. Oncotarget July 20 2016, Kovac et al. Nat Commun. Dec 3 2015 6:8940–9, Stratford et al. unpublished).

- OS cell lines with genomic aberrations in genes essential for the homologous recombination repair (HRR) pathways are sensitive to PARP-inhibition
- BMN 673 inhibits cell proliferation and cell viability (upper right) in an OS cell line with mutation in a key gene in HRR pathway apoptosis (lower right)
- The effect is not reversed when the drug is removed after 48 or 72 hours (below)







Conclusions:
Thorough studies of therapeutic targets in sarcoma patients and preclinical models should provide new therapeutic options to the clinic.
Both FGFR and PARP inhibitors are promising candidates.

Norwegian Cancer Society
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The Research Council of Norway