

## FDDC and UEF Launch PoI Project to Unlock New Opportunities to Modulate NRF2 for Future Therapeutic Applications

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Finnish Drug Discovery Center (FDDC) has initiated a new Proof-of-Idea (PoI) project in collaboration with the University of Eastern Finland (UEF) to assess the feasibility of developing inhibitors targeting NRF2, a transcription factor implicated in therapy resistance in multiple cancers.

A major challenge in the treatment of cancers is that tumour cells are either intrinsically resistant or acquire resistance during therapy. One of the key mediators of this resistance is the NRF2 transcription factor, which enables cancer cells to survive treatment-induced cellular stress by activating protective and adaptive pathways. Despite being overactive in many cancers, NRF2 has proven difficult to target pharmacologically.

The research group at UEF has identified a previously unknown site in the NRF2 protein that offers a new opportunity to modulate its activity in cancer cells. By targeting this site, it may be possible to weaken the stress-response capacity of tumour cells and improve their sensitivity to treatment. In addition to oncology, modulation of NRF2 activity may also have broader therapeutic relevance, as dysregulated stress-response pathways are implicated in diseases such as neurodegenerative disorders and inflammatory conditions.

The project is led by Professor **Anna-Liisa Levonen-Harju** from the A.I.Virtanen Institute for Molecular Sciences at UEF. Professor Levonen's group has extensive expertise in cellular stress biology and disease mechanisms, as well as established cellular models for evaluating candidate compounds. Professor Levonen's group is joined by Professor **Antti Poso** from UEF's School of Pharmacy, whose expertise supports the computational design and screening of candidate compounds.

In the project, advanced computational approaches, including large-scale virtual screening and molecular modelling, will be used to identify compounds that can interact with this newly identified site. The most promising candidates will then be experimentally tested to assess their biological activity and suitability for further drug development. The work will generate critical early evidence to evaluate the feasibility of targeting NRF2 through this novel mechanism.

The collaboration is supported through FDDC's Proof-of-Idea instrument, which invests in early feasibility studies for promising therapeutic targets. A successful outcome could provide the foundation for future drug discovery programmes aimed at overcoming therapy resistance in cancer and potentially enabling new therapeutic approaches in other disease areas.

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