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A c-Myc activation sensor-based high throughput drug screening identifies the anti-neoplastic effect of nitazoxanide

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Deregulation of c-Myc plays a central role in the tumorigenesis of many human cancers. Yet, the development of drugs that can regulate c-Myc activity has been challenging. To facilitate the identification of c-Myc inhibitors, we developed a molecular imaging sensor based high throughput-screening (HTS) system. This system uses a cell-based assay to detect c-Myc activation in a HTS format. Optimization of the assay performance in the HTS format resulted in uniform and robust signals at the baseline. Using this system, we performed a quantitative HTS against approximately 5,000 existing bioactive compounds from five different libraries. Thirty-nine potential hits were identified, including currently known c-Myc inhibitors. There are a few among the top potent hits that are not known for anti-c-Myc activity. One of these hits is nitazoxanide (NTZ), a thiazolide for treating human protozoal infections. Validation of NTZ in different cancer cell lines revealed a high potency for c-Myc inhibition with IC50 ranging between 10 - 500nM. Oral administration of NTZ in breast cancer xenograft mouse models significantly suppressed tumor growth by inhibition of c-Myc and induction of apoptosis. These findings suggest a potential of NTZ to be repurposed as a new anti-tumor agent for inhibition of c-Myc associated neoplasia. Our work also demonstrated the unique advantage of molecular imaging in accelerating discovery of drugs for c-Myc targeted cancer therapy.

Biography

Fan-Minogue H is a Bioinformatics Researcher in System Medicine at Stanford University. She has a MD, PhD in Cell Biology, MS in Bioinformatics. She has been working in the field of translational cancer research and devoted to better cancer therapy and patient outcome. Her research includes developing novel molecular imaging sensor systems to non-invasively monitor cancer signaling pathways and utilizing computational and statistic tools to analyze cancer genomics data for identification of new biomarkers and targets of cancer. She had a US patent on the c-Myc activation sensor system and welcome potential licenser.

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