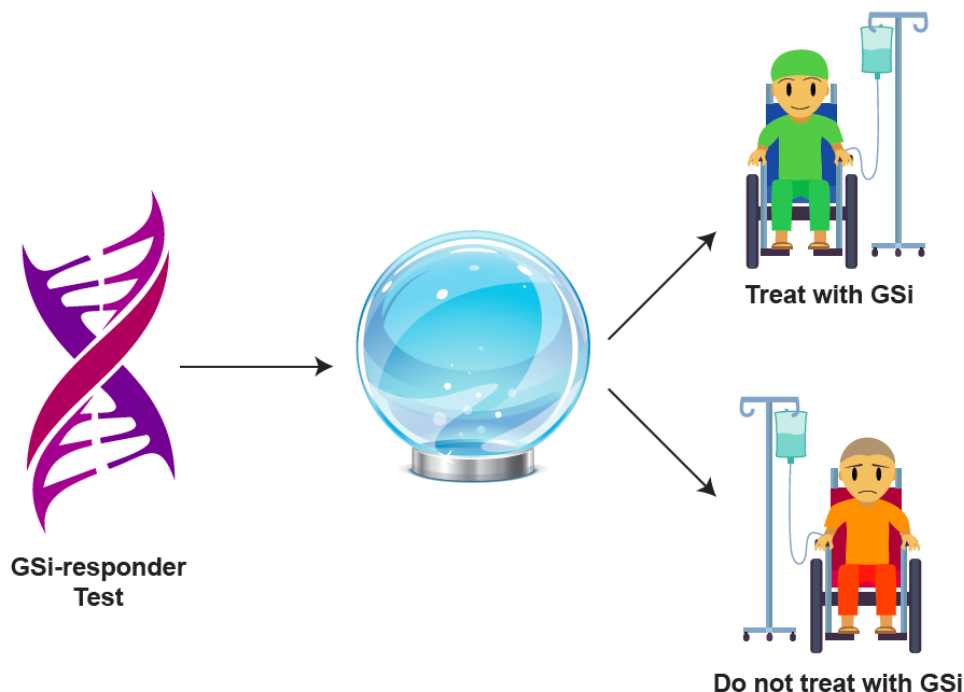


Novel pan-cancer predictor of gamma secretase inhibitor (GSI) sensitivity

- Identifying the right patients to maximize GSi therapeutic success



Background

Chemotherapy is an inevitability for a large proportion of cancer patients who are either diagnosed at late disease stage or develop recurrence following surgery. In practicality, however, the majority of agents are incapable of targeting key pathways (e.g. Notch signaling) fundamentally associated with advanced disease processes (e.g. stemness, metastasis, chemoresistance). This severely undermines the potential for disease stabilization in all cancer types. Reinvigorated by new generation compounds, improved dosing schedules and adverse effect (AE) management, gamma-secretase inhibitor (GSI)-based therapeutics now constitute a viable treatment avenue to improve progression-free survival (PFS) in patients. Nonetheless, successful adaptation of these drugs into routine clinical use will require robust biomarkers to identify patients who will benefit from such treatments while avoiding unnecessary treatment of those who will not.

The invention

Initially identified in a mouse model of GSi-sensitive biliary tract cancer, a 20-gene expression signature has been identified which can accurately predict sensitivity to multiple types of GSi compounds pan-cancer. Importantly, measuring the expression of this 'GSI responder signature' significantly outperforms measurement of GSi-target genes (originally used as criteria for patient inclusion in GSi clinical trials) in predicting therapeutic response.

Key selling points

- Enables personalized treatment for many advanced cancer types
- Mitigates risk of ineffective treatment in non-responder patients, avoiding unnecessary AEs and saving costs
- Predictive of sensitivity to all GSi-family compounds tested

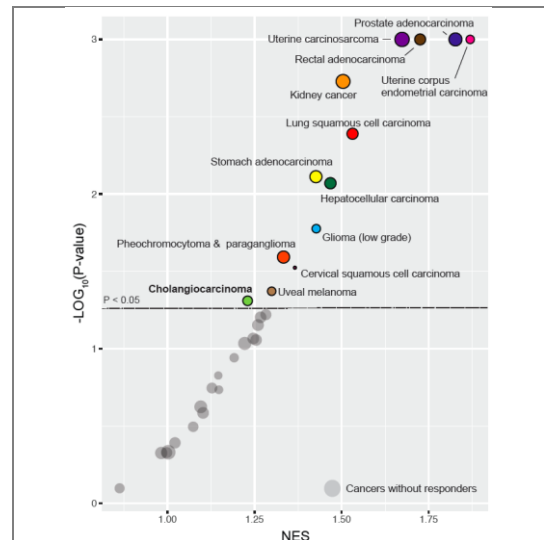
Development status

The GSi responder signature has been verified as a complete predictor of GSi sensitivity (AUC=1) across 60 diverse cancer cell lines *in vitro*. Pan-cancer analysis (31 cancers, 9409 tumors) of tumor profiles identified 41.9% cancer types to have large patient responder subgroups (32.6% - 59.6% patients within a given cancer type) who are predicted to be sensitive to GSi using our GSi signature.

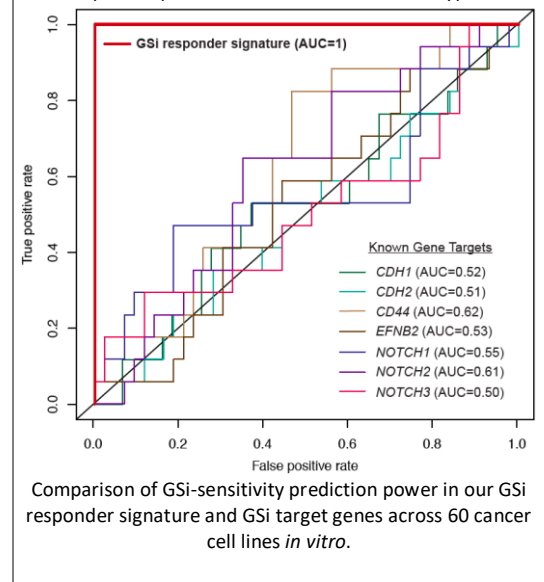
Ongoing work in collaboration with Herlev and Gentofte Hospital (Denmark) is establishing experimental trials using our GSi responder signature to select patients with diverse cancer types for GSi treatment

Intellectual property rights

Positive preliminary assessment, patent application to be drafted shortly



GSI responder signature-based identification of candidate responder patients across different cancer types.



Comparison of GSi-sensitivity prediction power in our GSi responder signature and GSi target genes across 60 cancer cell lines *in vitro*.