

Towards therapies that are designed to exploit biological cancer vulnerabilities



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Abstract

I will present our ongoing efforts to discover new cancer vulnerabilities and translate them into real-world therapies. We have developed a screening platform to isolate biological processes and interrogate their regulation and requirements. We have applied this strategy to the areas of oncogenic transcription and mRNA translation. This approach has identified new and surprising dependencies. For example, we discovered that the RNA helicase eIF4A is strictly required for the translation of mRNAs that carry multiple G-quadruplex elements in their 5'UTRs. These include all MYC RNAs and other oncogenic drivers. We developed small molecule inhibitors that show striking efficacy in vivo and are presently in clinical testing. Separately, we examined the requirements for oncogenic transcription factors. Our work on NRF2 has uncovered an unexpected requirement for the fructosamine-3 kinase (FN3K) that removes sugar adducts from proteins. We are presently developing inhibitors for this kinase and expect a therapeutic role in NRF2 driven solid tumors such as liver and lung cancers. The presentation will highlight our discovery process and the path towards new cancer therapeutics.

Biography

Hans-Guido Wendel is a tenured member of the faculty of Memorial Sloan Kettering Cancer Center. He trained in Medicine in Germany and Scotland and went to Cold Spring Harbor for scientific training before arriving at MSKCC in 2007. Guido's research has focused on the genetic drivers and therapeutic vulnerabilities in deadly cancers. He identified the RNA helicase eIF4A as a requirement for the translation of MYC proteins and developed small molecule inhibitors that show promise in clinical trials. Recently, he discovered protein deglycation as a vulnerability in NRF2 driven liver cancers and he is presently developing small molecule inhibitors to target this process. Guido's work has been published in top-tier journals and recognized with multiple awards, most recently the Harrington Discovery Award.