



Translational Sciences and Clinical Application

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Two major scientific challenges impede efforts to translate recent advances in our molecular understanding of cancer or other diseases to new medicines for clinical application. First, many cellular processes that represent clinically validated opportunities for the treatment of cancer are mediated by macromolecular assemblies, such as protein-protein interactions, which, are not routinely accessible to conventional methods for the identification of chemical leads. This curtails the repertoire of 'druggable' targets for intervention using small molecules. Second, limitations in our understanding of the biological effects of new agents impede their early clinical development. This makes it difficult to select appropriate clinical indications and drug combinations during the transition from Phase I to Phase II clinical trials, leading to an unacceptably high attrition rate. I will discuss new approaches we are developing to tackle these challenges, including new strategies to enlarge the 'druggable' target repertoire, to identify biomarkers for drug responsiveness, and to use this information in early-phase clinical trials. I will focus in particular on our work concerning three processes - DNA replication, repair and mitosis - that regulate the stability of cancer cell genomes.