S29-1 Fragment-Based Drug Discovery: Concept and Aim

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Fragment-Based Drug Discovery (FBDD) has been recognized as a newly emerged lead discovery methodology that involves biophysical fragment screening and chemistry-driven fragment-to-lead stages. Although fragments, defined as structurally simple and small compounds (typically <300 Da), have not been employed in conventional high-throughput screening (HTS), the recent significant progress in the biophysical screening methods enables fragment screening at a practical level.

The intention of FBDD primarily turns our attention to weakly but specifically binding fragments (hit fragments) as the starting point of medicinal chemistry. Hit fragments are then promoted to more potent lead compounds through linking/merging with another hit fragment and/or attaching functional groups. Another gift from attractive features of FBDD is ligand efficiency. Ligand efficiency is a useful guide in screening hit selection and hit-to-lead phases to achieve lead-likeness. Owing to this, a number of successful applications of FBDD into “undruggable” targets, where HTS and other lead identification methods failed to provide useful lead compounds, have been reported. As a result, FBDD is now expected to complement those more conventional methodologies.

This review presentation, as an introduction of the following lectures, will summarize the fundamental concepts of FBDD and will then discuss its advantages over other conventional drug discovery approaches.