MS03-1-2 From fragment screening to fragment growing - new methods for drug discovery
#MS03-1-2

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Abstract
Human glucokinase (GK) is a hexokinase isozyme (hexokinase IV) present in both the liver and pancreas. Glucokinase plays an important role in the phosphorylation of glucose to glucose-6-phosphate, which is a key step in glucose metabolism. In the beta cells of the pancreas, glucokinase acts as a glucose sensor for insulin secretion, while in the liver it facilitates the transformation of glucose into glycogen, which allows glucose to be stored for later use. The role of glucokinase in the reduction of glucose concentration leads to the pharmacological desire to develop glucokinase activators with the potential to counterbalance the glycaemic imbalance related to type-2 diabetes. Furthermore, applying fragment-based methods to identify fragment hits binding to glucokinase can lead to the recognition of allosteric activators of glucokinase, which can be used as lead compounds in the future. In combination with docking experiments, which aid the binding pose prediction, X-ray crystallography is utilised to understand the interactions between GK and its lead compounds.