

➤ The Service in Brief

The HitDetector is a service package which comprises biochemical testing of a drug-like small molecule library at one concentration in singlicate against a protein kinase of your choice selected from ProQinase's protein kinase panel. The customer receives a file with all 25,000 chemical structures and the screening results.

➤ The Library

- Source: commercial library provider
- No. of cpds: 25,000
- Quality: evaluated by highly experienced medicinal chemist
- Positive control: Staurosporine (4x included)
- Purity: >90%
- Range of MW: 200 - 500 (see Figure 1)
- Druglikeness: complies with Lipinski's rule of 5
- Patentability: checked at time of library synthesis

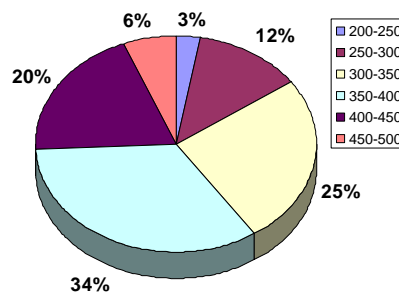


Figure 1: MW range distribution

➤ Example of Application

In an internal evaluation project, the library was tested at a concentration of 10 μ M on ProQinase's HTS robot system against 4 different protein kinase targets. Every compound exhibiting more than 60% inhibition against at least one of the 4 kinases was defined as a primary hit. The total primary hit rate was about 1.4% (349 cpds). In subsequent confirmation assays, IC₅₀ values below 30 μ M were found for 249 primary hits.

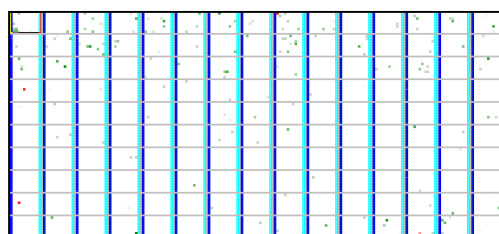


Figure 2: Distribution of hits on 150 plates

➤ Further Development: From Hit to Preclinical Candidate

ProQinase offers partnership for *Integrated Cancer Drug Discovery Projects* in order to develop your primary hits further from hit to lead and subsequently to a preclinical candidate. All biological testing is available in house at ProQinase and chemical optimization will be performed in collaboration with first-class chemistry partners. ProQinase has longstanding relationships with Mercachem (www.mercachem.com) and Novalix (www.novalix-pharma.com).

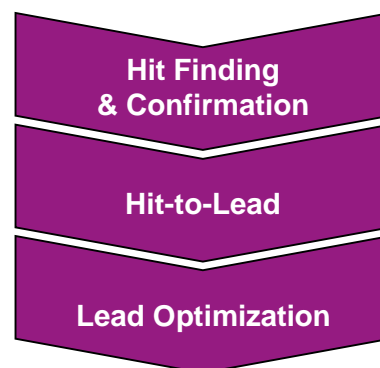


Figure 3: Drug development phases