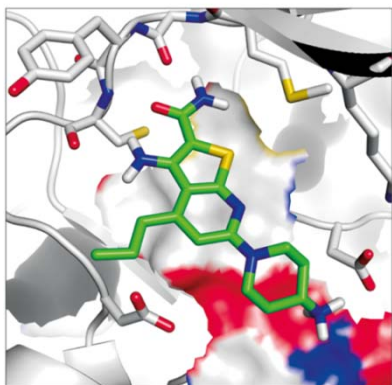




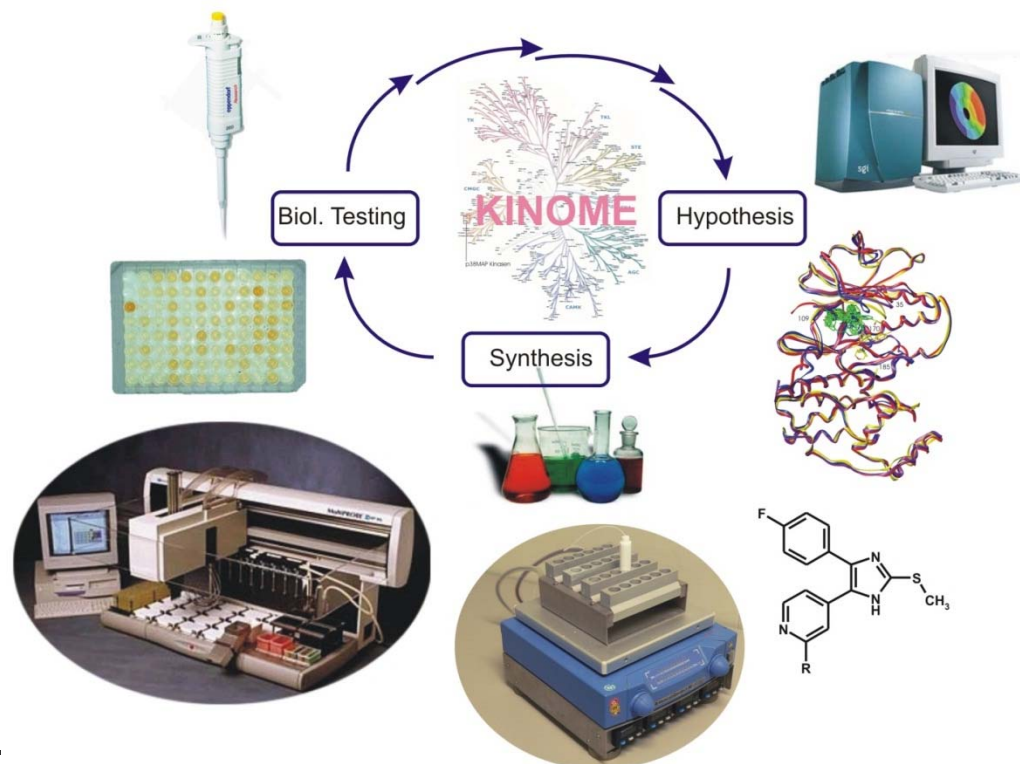
RSC Drug Discovery

Edited by Jeremy I Levin and Stefan Laufer

**Anti-Inflammatory  
Drug Discovery**



**Medicinal Chemistry and early Drug Discovery**  
**Structure-based design, hit to lead to candidate**



**Targets:**

**Proteinkinases p38 $\alpha$  and  $\delta$ , JNK3, JAK3, EGFR- mt/mutants  
GSK3 $\beta$ , Aurora Activating Protein, MKKs  
mPGES1, LOXs  
PI3K $\gamma$**



**CADD: Structure-based design, database-mining**

**Synthesis: Hit-Lead-Candidate:  
MedChem, Resin-based Parallel synthesis**

**Primary screen: Enzyme assays, cell-based assays,  
humane whole blood based assays**

**In vitro metabolism: Isolated CYPs, Liver microsomes, Liver homogenate  
(rat and human)  
Metabolic stability: human whole blood, liver homogenate**

**Equipment: IR, NMR, GC-MS, LC-MS (Ion trap, Triple Quad), Maldi-TOF**

**Personel experience: „Proof of concept“ up to Phase IIa**



**25 years experience in medicinal chemistry, 10a industry, 15a academia**  
**Small molecules, inflammation and autoimmun diseases (RA, IBD, COPD, Psoriasis)**

**Tailormade „non high threwhput“ discovery and optimization projects**

**Structure based design, hit to lead to candidate**

**strongly IP oriented, > 40 patent families, > 300 national applications**

**2 clinical developments (Licofelone P III, CBS-3595 P I)**

**4 preclinical candidates: - CNS-permeable p38, Alzheimer, Pain**

**- 3rd gen. p38, HCC**

**- Moguntinone (VIP-Program BMBF, Uni Mainz)**

**- p38-Inhibitors, dermal application (Interleukin-Genetics)**

**4.000 compound proprietary library for proteinkinase inhibitors**

**(1600 available via ChemBioNet screening port)**

**1.000 dto. eicosanoid-inhibitors (COX-1,2,3, LOXs, mPGES1, cPLA<sub>2</sub>)**

**New projects: Kinase-Inhibition in Alzheimer and other CNS-diseases**

**Mutant-selective Kinase-Inhibitors in Cancer**

**Kinase-Inhibitors from natural sources**

**mPGES1/5-LOX Inhibitors (3rd generation NSAIDs)**

**PI3K $\gamma$  (p101/110 $\gamma$ ), Type II PI3Ks**

**MKKs, Aurora**