Christian Ottmann, Med chem 2013, 3:4
http://dx.doi.org/10.4172/2161-0444.S1.009

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Medicinal Chemistry & Computer Aided Drug Designing

October 15-17, 2013 Hampton Inn Tropicana, Las Vegas, NV, USA

# Small-molecule stabilization of 14-3-3 protein-protein interactions

**Christian Ottmann**
Eindhoven University of Technology, Netherlands

Targeted pharmacological modulation of protein-protein interactions (PPIs) is a promising strategy in chemical biology and drug development. However, in the vast majority of cases this concept has been realized only for inhibition of PPIs despite the fact that in many biomedical contexts stabilization of PPIs would be desirable. The natural product fusicoccin A is stabilizing the binding of 14-3-3 adapter proteins to the plant H+-ATPase PMA serving as proof-of-principle molecule for the possibility to address the widespread interactome of 14-3-3 proteins. In humans, these proteins interact with partner proteins implicated for example in cancer (p53, Raf, YAP/TAZ, β-catenin) or neurodegenerative diseases (Tau, α-Synuclein, LRRK2). We have devised a fusicoccin-derivative (FC-THF) that stabilizes the interaction of 14-3-3 with the K+ channel TASK-3. Protein crystallography shows how this molecule binds to the rim of the interface of 14-3-3 proteins and a TASK-3-derived phosphopeptide contacting both protein partners simultaneously. Since binding of 14-3-3 proteins mediates trafficking of TASK-3 to the plasma membrane administration of FC-THF enhances surface expression of the channel in cells and increases K+ currents. Together with the demonstration that 14-3-3 PPI stabilizers can be identified by screening conventional compound libraries these studies support the concept of small-molecule PPI stabilization for biomedical research. In addition we have also shown that inhibition of 14-3-3 PPIs is a feasible approach in certain physiological settings.

## Biography

Christian Ottmann has completed his Ph.D. from the University of Tuebingen (Germany) and postdoctoral studies from the Max Planck Institute of Molecular Physiology (Dortmund, Germany). He is currently Associate Professor at Eindhoven University of Technology (The Netherlands). He has published more than 50 papers in reputed journals and has been serving as a guest editor for several special issues on the modulation of protein-protein interactions.

christian.ottmann@mpi-dortmund.mpg.de