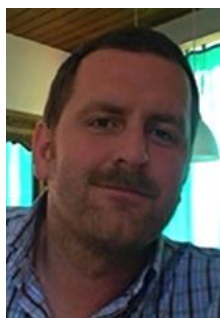


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***In vivo* bioassays based on model organisms to identify biomedically relevant marine metabolites**

Emerging challenges within the current drug discovery paradigm are prompting renewed interest in secondary metabolites as an attractive source of novel, structurally diverse small molecules that have been evolutionarily 'pre-selected' for bioactivity. With the recent validation of zebrafish as a biomedically relevant model for *in vivo* drug discovery, the zebrafish bioassay-guided identification of natural products is an attractive strategy to generate new lead compounds in a number of indication areas. We have recently developed a number of *in vivo*, microgram-scale, high-throughput bioassays based on zebrafish embryos and larvae for the systematic identification and pharmacological characterization of bioactive natural products. Zebrafish offer the ability to rapidly evaluate – at a very early stage in the drug discovery process – not only the therapeutic potential of natural products, but also their potential hepato-, cardio-, and neurotoxicities. Due to the requirement for only microgram quantities of compounds, *in vivo* assays based on zebrafish are useful not only for bioassay-guided isolation, but also for the subsequent derivatization of bioactive natural products to generate drug discovery leads. Recent progress within the EU FP7 project PharmaSea is revealing the potential of zebrafish-driven biodiscovery to identify neuroactive secondary metabolites from marine microorganisms.