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CHEMBIOCHEM

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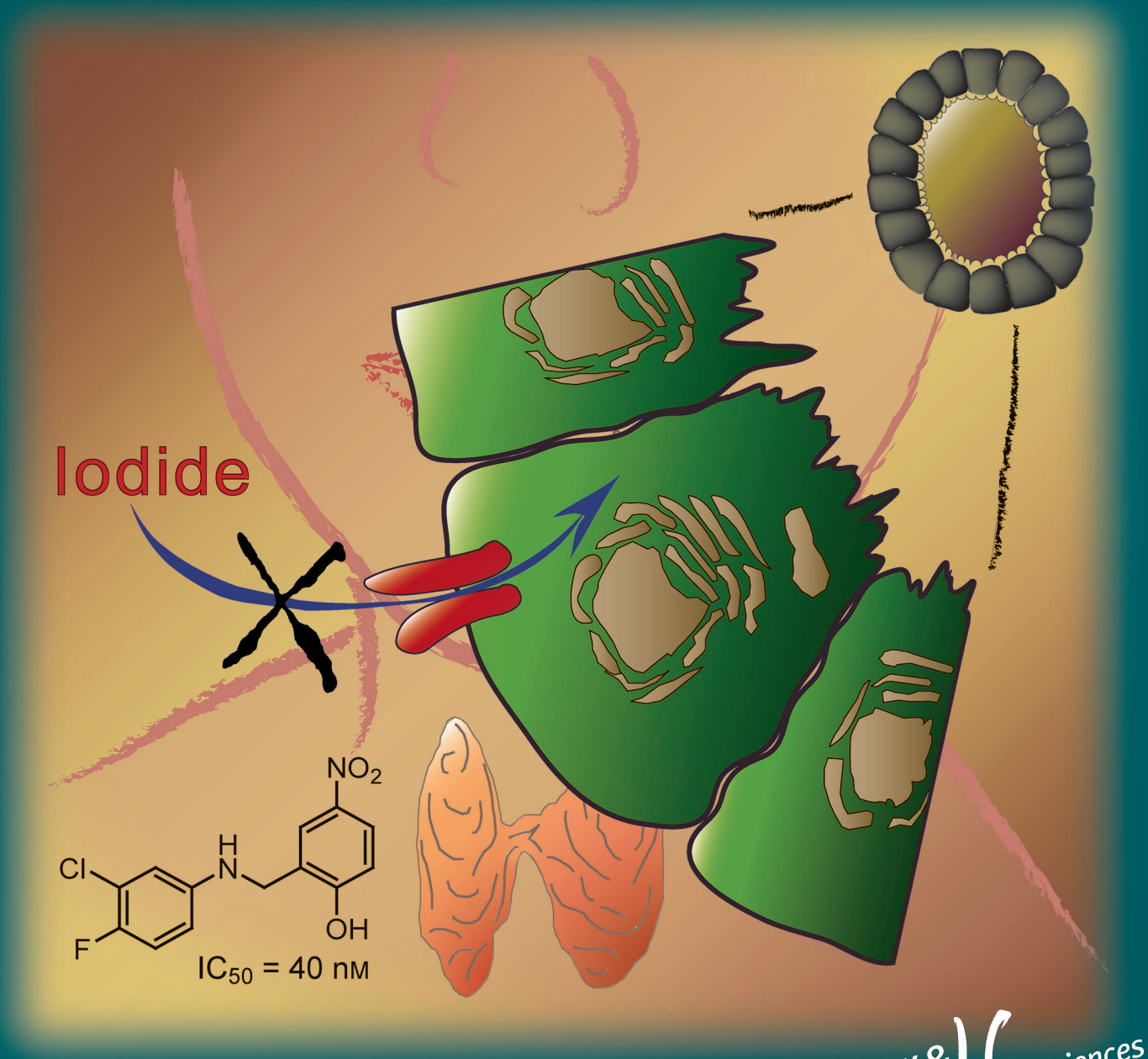


Chemistry & Life Sciences

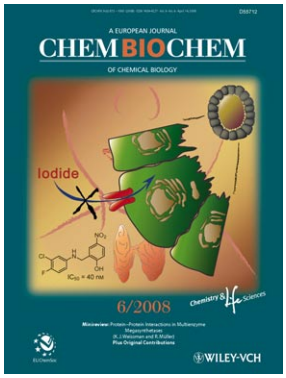
6/2008

Minireview: Protein–Protein Interactions in Multienzyme Megasynthetases
(K. J. Weissman and R. Müller)
Plus Original Contributions

EUChemSoc

WILEY-VCH

Cover Picture



Nathalie Lecat-Guillet, Goulven Merer, Roman Lopez, Thierry Pourcher, Bernard Rousseau, and Yves Ambroise*

The cover picture shows a thyroid follicular cell involved in basolateral iodide uptake. This transport is mediated by the Na/I symporter (NIS) and represents the first step in the biosynthesis of thyroid hormones T3 and T4. High-throughput screening has identified novel small-molecule inhibitors of iodide uptake with potencies in the nM range. Biological activities were consolidated by detailed isotopic flux experiments. Time–dependent radioiodide uptake has provided the first mechanistic information on the mode of action of these inhibitors. The data indicate that they act through distinct mechanisms, either by direct NIS disruption or by altering the post–translational pathways involved in iodide uptake. These small organic molecules are of both physiological and clinical importance. They represent pharmacological tools for the characterization of NIS trafficking and activation mechanisms. They also offer considerable opportunities for the treatment of thyroid dysfunction. Further details can be found in the article by Y. Ambroise et al. on p. 889 ff.