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Impact of novel lipidized analogs of neuropeptides on food intake decrease and metabolic changes in rodents

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Obesity is a frequent metabolic disorder but an effective therapy is still scarce. Anorexigenic neuropeptides seem to be potential specific tools for obesity treatment but their peptide character complicates their delivery to the brain, necessary for their central effect, and makes them subjects of fast degradation. In order to overcome the unfavorable facts mentioned, lipidization of anorexigenic neuropeptide prolactin-releasing peptide (PrRP) whose strong anorexigenic effect was demonstrated with the fact that both PrRP and its receptor knock-outs resulted in obese phenotypes, was applied. Analogs of PrRP with attached fatty acids showed unabated biological activities compared to the native PrRP regarding binding affinity and signaling in cells expressing PrRP receptor. Most interestingly, these analogs revealed a strong and long-lasting anorexigenic effects after their peripheral administrations to fasted mice and rats and neuronal activation in brain areas involved in food intake regulation. Moreover, repeated subcutaneous administration of palmitoylated PrRP lowered food intake and body weight and improved metabolic parameters in diet-induced obese mice. For the anorexigenic effect of native PrRP, central administration was necessary. Lipidization of PrRP enabled its peripheral administration for its anorexigenic effect in the brain, most probably by enhancing its stability in the blood and mediating the peptide to cross the blood brain barrier.

Biography

Lenka Maletinska received her PhD from the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic and her post-doc training from University of Sherbrooke, Quebec, Canada and Lawrence Berkeley Laboratories, Berkeley, California. Recently, she is the head of the group Antiobesity peptides at the Institute of Organic Chemistry and Biochemistry, Prague, Czech Republic. Her research interests focus on peptides involved in food intake regulation and mechanisms of their action. She published over 40 articles in peer-reviewed journals. She is a member of European and American Peptide Society and editorial board member of JOE and JME.

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