

### 53. UNCOUPLING AGENTS AND THEIR BIOMEDICAL ROLES

**Author:** Curnic Andreea

**Scientific adviser:** Tatiana Timercan, MD, PhD, Associate Professor, Department of Biochemistry and Clinical Biochemistry, *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova.

**Introduction.** Uncoupling agents, or uncouplers, are molecules, which are classified as ion transporters, located in the internal membrane of mitochondria. They discharge the proton gradient, which is generated by the respiratory chain, by transporting hydrogen ions. As a result, ATP-synthetase cannot be activated due to the lack of that gradient, thus the oxidative phosphorylation is "uncoupled" from the electron transport chain. Therefore, the energy used for ATP synthesis is dissipated in heat, which explains the main role of thermogenesis. There are 2 types of uncouplers: natural, which are UCPs (short for Uncoupling Proteins) and synthetic, which have an importance in research and not only.

**Aim of study.** Exploring the roles and flaws of the uncoupling agents and the factors which increase their activities

**Methods and materials.** Selected from articles, found in databases (PubMed, NCIB, Google Scholar, etc) according to the keywords "uncoupling", "uncoupling agent", "oxidative phosphorylation".

**Results.** The most known and most studied uncoupling agent at the moment is thermogenin (UCP 1), which is present mostly in the brown adipose tissue in newborns and hibernating mammals. It is also involved in energetic balance due to its involvement in uncoupling oxidative phosphorylation from the respiratory chain. The main stimulating factor of thermogenin is exposure to cold temperatures. Besides thermogenesis, uncoupling agents have significant roles even in other organs. For example, in the nervous system, they stimulate the transport of calcium ions outside mitochondria, thus avoiding neuronal hyperexcitability, which is a key feature in epilepsy. Also, they help the neuronal tissue recover from injuries. Another interesting effect scientists noticed about uncouplers is weight loss. Dinitrophenol, a synthetic uncoupling agent, was used as a miracle pill for losing weight in the 1930s until FDA illegalized it in 1938 due to severe side effects. The increase of an uncoupling protein can inhibit beta cells from endocrine pancreas to synthesize insulin, leading to their dysfunction or even to type 2 diabetes. Another point about the uncouplers is that the main factors that increase their activities are free fatty acids and thyroid hormones.

**Conclusion.** Uncoupling agents are not only molecules that generate heat, but have a major influence towards some processes such as neuronal excitability, insulin synthesis, weight loss and so on. At the moment, the scientists are still studying the recently discovered uncouplers, whose roles are still unknown.