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A putative mechanism of the Sodium/Iodide Symporter regulation during repetitive administration of stable Iodide described by a Systems Biology approach

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Abstract

A single dose of potassium iodide (KI) against a prolonged exposure to repeated radioactivity might not be effective enough to protect the thyroid. Our group have shown that a repetitive dose of KI for eight days offers efficient protection without adverse effects in male rats [1].

However, we also have shown that the expression of the genes involved in the Wolff-Chaikoff effect changes during this period. Notably, a decrease in the sodium/iodide symporter (*nis*) gene expression has been observed [1]. This effect may result in hypothyroidism due to a decrease in thyroid hormones.

NIS is responsible for the uptake of KI and thus plays an important role in the Wolff-Chaikoff effect. The mechanism of a single dose of KI on the toxicity of the thyroid is well known [2], in contrast to repetitive administration of KI for eight days.

In the present study, we try to understand the Wolff-Chaikoff regulation and its molecular constituents during repetitive administration of KI. For this purpose, we have constructed manually a biochemical reaction network that is visualised as a "geographical" map of a single thyrocyte cell depicting the iodide and thyroid hormone metabolism. In order to investigate any regulation circuits of *nis*, Cytoscape and the plugin BiNoM [3, 4] were used to perform path analysis of the network to investigate if a path exists from the node iodide going to the node representing "nis transcription". Subsequently, sequential network reduction has led to final model that might explain a putative mechanism behind *nis* regulation and repetitive iodide administration.

In addition, this map reviews the most-update information about iodide and thyroid hormone metabolism. Besides as a source of information, it can help to elucidate the mode of action of KI on gene transcription after repetitive KI administration.

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