Researchers generate thyroid tissue using mice stem cells

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(Medical Xpress)—Researchers in Brussels, with assistance from U.S. colleagues, have succeeded in generating thyroid tissue using mice embryonic stem cells. A procedure involving grafting new tissue onto a disabled thyroid resulted in restored function for nine out of ten study mice, the team reports in their paper published in the journal *Nature*.

The thyroid is an endocrine gland found in the neck. It functions to control how quickly the body uses energy, and to produce certain proteins. It also has a role in regulating the responsiveness of other hormones. It does its job by producing thyroid hormones—if the thyroid is damaged or grows abnormally, a condition known as hypothyroidism results. This condition causes reduced production of the hormones that allow for normal body growth and mental development.

To cure the condition, researchers have turned to organ regeneration, a process where stem cells are manipulated into growing new organ cells. The process of thyroid regeneration is complicated by the requirement that cells grow in a physically-optimal shape. Such a shape has spherical follicles that trap iodide and hold it until a concentration threshold is reached.

To address this challenge, the researchers took stem cells from mice embryos and genetically altered them to express the two proteins NKX2-1 and PAX8, which are normally only expressed together in the thyroid. To cause the follicles to develop, they exposed the cells to the hormone thyrotropin in a petri dish, which resulted in the cells

developing into three dimensional structures with follicles similar to those found in a healthy thyroid.

Because of the promising results found in the first stage of their work, the researchers grafted newly grown tissue into mice that had been caused to have hypothyroidism, and found that nine out of ten experienced full recoveries.

More work will have to be done in this area to determine any undesirable side effects before human test trials can be conducted. However, at this stage, the researchers report that the procedure looks very promising, offering hope to those who have lost function due to infections, drug use, or radiation treatments.

More information: Generation of functional thyroid from embryonic stem cells, *Nature* (2012) doi:10.1038/nature11525

Abstract
Author information Supplementary information
The primary function of the thyroid gland is to metabolize iodide by synthesizing thyroid hormones, which are critical regulators of growth, development and metabolism in almost all tissues. So far, research on thyroid morphogenesis has been missing an efficient stem-cell model system that allows for the in vitro recapitulation of the molecular and morphogenic events regulating thyroid follicular-cell differentiation and subsequent assembly into functional thyroid follicles. Here we report that a transient overexpression of the transcription factors NKX2-1 and PAX8 is sufficient to direct mouse embryonic stem-cell differentiation into thyroid follicular cells that organize into three-dimensional follicular structures when treated with thyrotropin. These in vitro-derived follicles showed appreciable iodide organification activity. Importantly, when grafted in vivo into athyroid mice, these follicles rescued thyroid hormone plasma levels and promoted subsequent symptomatic recovery.

Thus, mouse embryonic stem cells can be induced to differentiate into thyroid follicular cells in vitro and generate functional thyroid tissue.