ARTICLE IN REVIEW:

3D human thyroid microtissue model for chemical screening

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TITLE: Development of an *In Vitro* Human Thyroid Microtissue Model for Chemical Screening.

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STUDY DESIGN: Benchtop

SUMMARY: Currently, drug safety and efficacy, chemical toxicity, and other important types of testing are performed in either animal models or two-dimensional (2D) cell cultures. These 2D methods do not always accurately mimic human tissue and may lead to unsafe products coming to market or, conversely, the failure to recognize a promising new drug due to a testing model which fails to fully represent human tissues or organs. One potential solution is to use three-dimensional (3D) cell cultures which more closely mimic human tissues. This paper reports the development of a 3D-reconstructed all human thyroid microtissue model to evaluate the potential toxicity of chemicals on thyroid hormone (TH) production and secretion. The 3D thyroid microtissue model restored TH synthesis absent in 2D culture, which could be effectively blocked by known inhibitors. Thus, this type of 3D organotypic microtissue model can be used to test tissue-level effects of chemicals, potentially replacing 2D cell culture and/or animal models.

More differentiated phenotype:

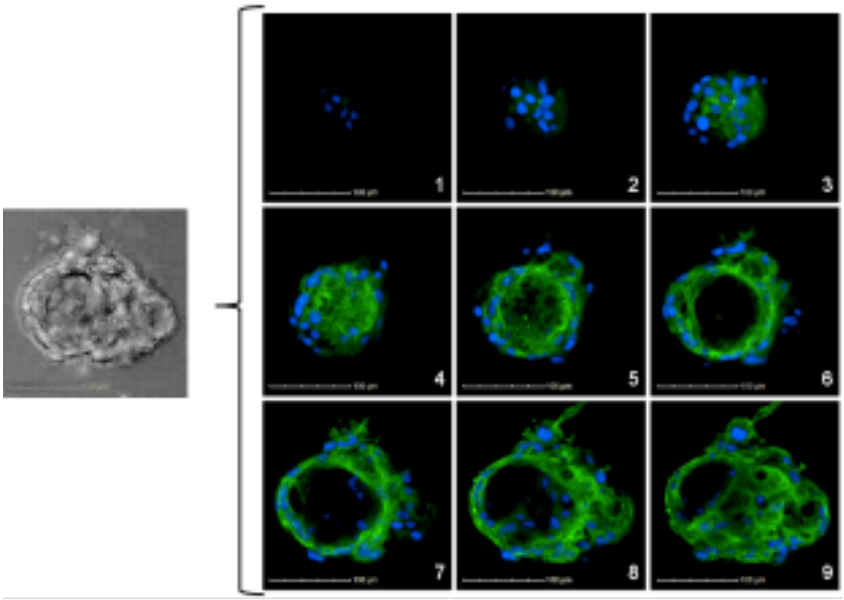
3D-reconstructed thyrocytes exhibit genetic and protein expression critical for TH production and characteristic of a more differentiated state compared to 2D cultures.

Physiologic follicle-like morphology:

Upon stimulation, 3D-reconstructed thyrocytes organize into a native follicle-like architecture.

Effective model for chemical screening:

Physiologic TH synthesis was restored in the 3D-reconstructed model. Known inhibitors blocked TH synthesis, validating this model for chemical screening.



Follicle-like morphology of 3D thyroid microtissue

Follicle-like morphology of a 3D microtissue at day 10 of culture visualized with confocal microscopy. Panels 1-9 are a bottom-to-top visualization of a single microtissue.

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