

# Adult thyroid stem cells as a novel source of brown adipose tissue: clues to bioengineered rat models of tissue implants for innovative treatment of obesity

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Brown adipose tissue (BAT) can provide a novel therapeutic to treat obesity. Using adult male rat, thyroid stem cells (TSC) recently isolated by our group we have studied their differentiation potential to BAT as a cell source to engineer metabolically-active biomaterial-based tissue implants. TSC were obtained as colony forming unit-like cultures [1] whereas adipose differentiation was reached based on a protocol with 4 cycles (6 d/cycle) of white adipogenic induction. Presence of lipid droplets was assessed by light microscopy (LM) using oil red O histochemistry, their ultrastructural morphology studied by TEM, and difference in the 3D cellular morphology screened by SEM. Finally, a morphometric analysis was conducted with LM to determine the contribution of different cell phenotypes at control and differentiated levels, and their relevant subcellular features. More than 90% of control, adult TSC displayed a multipolar morphology, and flattening at increasing times as opposed to less than 10% of cells that were fibroblastoid. Similar, adipoblast-like cells exhibited a multipolar and, less frequently fibroblastoid morphotypes characterized by the absence of intracellular triglycerides. In contrast, white preadipocytes were identified as multipolar and ovoid cells containing small lipid droplets fusing into bigger ones. Differently, brown preadipocytes displayed a multipolar filamentous-rich phenotype, with abundant lipid droplets around 50% less in size than those of the white counterpart. Finally, few mature brown adipocytes were observed, depicting a polygonal shape with a central nucleus surrounded by sizeable lipid droplets, and a nucleus/cytoplasm ratio lower than that of all preadipocytes. At 21 days of induction, 70% of adipoblast-like cells were replaced by white preadipocytes; however, brown preadipocytes increased in number throughout the differentiation time, reaching 14% of all cells at 28 days. Our results show that adult male rat TSC have a remarkable potential to differentiate in culture to the brown lineage even in the absence of specific browning stimuli, providing an innovative source to engineer metabolically-active bioimplants for the treatment of obesity.

## References

- [1] Barbaro et al (2013). Adult stem/progenitor cells of the rat thyroid: side population distribution, intermediate filament expression, and long-term in vitro expansion. *I.J.A.E* 118, (suppl 2) 19.

## Key words

Adult Thyroid Stem Cells, BAT, Bioimplant, Obesity.