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The effect of thyroid hormone substitution on M/L-cone development in *in vitro* organotypic retinal culture

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The retina of most mammalian species contains two types of cones, one population being sensitive to shorter wavelengths (S-cones), and another one with the a peak sensitivity in the green or in the red part of the spectrum (M/L-cones). According to the widely accepted theory of transdifferentiation, these two populations do not develop independently from each other. All cones first express the S-opsin only, and some of them continue to do so till adulthood (genuine S-cones). The rest of the cones switch on M/L-opsin production as well, coexpress both pigments for a limited time interval (transitory photopigment coexpression), then S-opsin disappears from their inner segments. Despite intensive studies, little is known about the factors influencing this pigment switch. The putative candidates (e.g.: thyroid hormones, retinoic acid, growth factors and their receptors) are numerous, their precise role however is mostly unknown.

The most common animal models to study the possible regulatory factors are based on rat and mouse retinas. The disadvantage of all these approaches is that these species have at least two cone populations, thus each factor may independently influence the development of both cone types, and their interaction may also modify the results. In the mouse a dorso-ventral gradient could also be detected in the expression of opsin types, making the interpretation of the results even less reliable.

Hereby, we suggest a new model animal to study the possible regulatory factors of M/L-cone differentiation. The Syrian golden hamster as reported here possesses a retina that is devoid of genuine S-cones. The one single cone population expresses the M/L-pigment only, an ideal situation for developmental investigations. The retina also exhibits full differentiation even in vitro organotypic retinal cultures, under control conditions. Analyzing and comparing the retinal development of this species in vivo and in vitro, under different culturing conditions allow us to estimate the effect of regulatory factors in a homogeneous cone system. The first series of experiments reported here, focused on thyroid hormones that were known to play a decisive role in mouse M/L-cone development.

For in vivo retinal culturing retinas of Syrian golden hamsters (D0-4) were explanted onto a semiporous membrane and cultured till D14. The culturing media contained DMEM and HEPES (1:1) supplemented by hormones and vitamins, with or without serum (10% FCS) added. After fixation, the retinas were analyzed by immunocytochemistry.

Our results show that unlike in the mouse, thyroid hormone deprivation does not influence M/L-cone differentiation in the Syrian hamster. In all types of media, both supplemented with, or devoid of thyroid hormone M/L-cones were detectable in comparable quantity and exhibiting similar morphology. In serum free medium, on the other hand, practically no M/L-cones were present, and differentiation was not completed even when hormone was substituted in excess. These results demonstrate that some unknown factor - rather than thyroid hormone - is present in the serum that is necessary for cone differentiation in the Syrian golden hamster, indicating that cone development may be controlled by a different mechanism in this species.

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