SUMMARY
The photoperiodic response of the gonads requires T₃, which is generated photo-periodically from T₄ by type 2 iodothyronine deiodinase in the hypothalamus. Although thyroid hormones were long thought to traverse the plasma membrane by passive diffusion due to their lipophilic nature, it is now known that several organic anion transporting polypeptides (OATP) transport thyroid hormones into target cells. In this study, the authors have used database searches to isolate DNA sequences encoding members of the chicken OATP family and to construct a molecular phylogenetic tree. Comprehensive expression analyses using in situ hybridization revealed strong expression of “cOATP1c1” and weak expression of “cOATP1b1” in the ventro-lateral walls of basal tuberal hypothalamus, whereas expression of four genes (cOATP1a1, cOATP1b1, cOATP1c1, and cOATP3a2) was observed in the choroid plexus. Expression levels of all these genes in both regions were not different between short-day and long-day conditions. Functional expression of cOATP1c1 in Chinese hamster ovary cells revealed that cOATP1c1 is a highly specific transporter for T₄ with an apparent Km of 6.8 nM and Vmax of 1.50 pmol per milligram of protein per minute. These results suggest that cOATP1c1 could be involved in the thyroxine transport necessary for the avian photoperiodic response of the gonads.

COMMENT
How many among you were aware that thyroid hormones play a role in the reproduction of birds? Well, I was not. And I was amazed to learn that the initial observation for a pivotal role of thyroid hormones in such reproductive processes was made more than thirty years ago in starlings. Most birds living outside the tropics use changes in day length to time their breeding seasons. The same group of investigators has shown previously that the type 2 iodothyronine deiodinase (Dio2) generated T₃ photoperiodically in the hypothalamus of Japanese quail and that this specific hormone production was critical for the photoperiodic response of the gonads in these birds. In the present article, the authors focus on the thyroid hormone transporting system that seems to play a key role in getting thyroid hormone into target cells. In recent years, a family of proteins that facilitate transport of thyroid hormones across the cell membranes has been identified and characterized in mammalian species. The transporters belong to the OATP family (organic anion transport polypeptides) and the identification of this novel family raises an entirely new class of genes/proteins that may influence thyroid hormone function. Following the sequencing of the chicken genome, the analysis of avian OATPs has been made possible, and the present study represents the first comprehensive analysis of avian OATPs. Using a database search, the authors have identified 10 chicken OATP genes. Japanese quails are highly photoperiodic and exhibit a form of seasonal photo-refractoriness. Thus, the photoperiodic regulation of reproduction in these birds provided a good basis to investigate thyroid function in relation to the regulation of reproduction. The authors
identified the expression of four OATP genes in the choroids plexus and of even more interest of two genes in the hypothalamus. The tuberal region of the hypothalamus is precisely the same part of the brain where they had previously shown the photoperiodic regulation of Dio2, with the induction of the production of T_3_. The main message of this study is that there is a high expression of a specific T_4_ transporter, precisely in the brain area which was previously identified to be a key site of thyroid hormone action for the regulation of the photoperiodic sexual response in quail. However, the authors could find no evidence for photoperiodic regulation of the OATP genes, by keeping the birds on long-day versus short-day conditions. Therefore, we will have to wait for future studies to see whether there are qualitative species differences in the degree to which different aspects of the thyroid hormone system are modulated in relation to the regulation of the photoperiodic response in seasonally breeding species.

These comments were largely inspired by the Editorial written by Gregory F. Ball, accompanying the publication of this article. (Daniel Glinoer MD, PhD)

See Figure below

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**Fig. 1.** Phylogenetic tree of the Oatp superfamily. The tree was generated using the ClustalW program (11) and drawn with TreeView (12). Branch lengths are drawn to scale. GenBank accession numbers and proposed protein names for chicken Oatps are underlined. Human OATPs are written in capital letters. mOatp and rOatp indicate mouse and rat Oatps, respectively.

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