行政院國家科學委員會專題研究計畫　成果報告

血型抗原 I 基因，成人 i 血型與先天性白內障(3/3)

計畫類別：個別型計畫
計畫編號：NSC92-2314-B-002-239-
執行期間：92 年 08 月 01 日至 93 年 07 月 31 日
執行單位：國立臺灣大學生化科學研究所

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報告類型：完整報告

處理方式：本計畫可公開查詢

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The aims of this project are to: 1) establish the molecular genetics background of, and the relationship between, the human *I* β6GlcNAcT gene locus and congenital cataracts; 2) identify and articulate the molecular mechanism of the *I* gene mutation for the development of lens opacity; and 3) to establish the mechanism and functional role of I carbohydrate structure and I β6GlcNAcT activity for maintenance of lens transparency.

Cataracts are the leading cause of vision impairment worldwide. Consequently, much effort has been devoted to the study of the molecular genetics of cataracts, the mechanisms through which lens transparency is maintained, and the establishment of mouse models for cataract research. So far, human gene loci which have been identified as responsible for cataracts can be classified into four main categories: structural (*e.g.*, crystallins and cytoskeletons); redox (systems which minimize oxidative damage); osmotic (transporters which maintain osmotic balance); and systemic (associated multisystem disorders).

To date, no associations have been reported between any glycosyltransferase and cataract formation. Identification of the molecular mechanisms proposed in this project would enhance our understanding of the mechanisms involved in cataract formation and further identify the novel structure and the novel molecule essential for maintenance of lens transparency.

Results

1. The genomic organization of the human *I* locus was revealed, and the cDNA sequences of the three *IGnT* structures were elucidated by RACE

analyses.

2. The expression profiles for the *IGnT* gene from various human tissues were inspected.

3. The *IGnT* gene structures of the adult i whites (without congenital cataracts) and the adult i Taiwanese (with congenital cataracts) were analyzed. Wild-type *IGnTA* and *IGnTB* but mutant *IGnTC* are present in the adult i whites without congenital cataracts All three *IGnT* forms of the adult i Taiwanese individuals with congenital cataracts were mutated

4. Activity of the enzymes encoded from the mutant *IGnT* genes was determined.

5. A defect in *IGnTC* gene function leads to the absence of I antigen in RBCs, whereas congenital cataracts occur in those i adults where all three IGnT-enzyme functions are defective, but not in analogs where only the *IGnTC* form is defective.

6. *IGnTC* is the only one of three *IGnT* transcripts expressed in reticulocytes, whereas only the *IGnTB* transcript is expressed in lens-epithelium cells. This result indicates that the *IGnTC* is the gene responsible for the formation of the I antigen on red blood cells.