摘　要

因感光細胞退化而造成失明的人類先天色素性視網膜炎中，視網膜神經網絡會出現重塑現象。在利用 RCS 大鼠作為人類色素性視網膜炎的模式動物之研究報告指出，因感光細胞退化晚期所造成之重塑會使內核層細胞與節細胞發生嚴重重組現象。現今色素性視網膜炎的治療方法均是基於殘存神經細胞的功能仍然完好，忽略退化晚期的重塑現象。然而，因為鮮少有針對退化晚期視網膜節細胞特性的研究，故本篇研究希望以形態與電生理的方式描述視網膜節細胞於退化晚期之特性。研究利用出生後 331 至 418 天、526 至 575 天的 RCS 大鼠與兩種正常大鼠（SD 及 LE），比較其視網膜節細胞在形態是否有差異，另外在 RCS 及 SD 大鼠上也進行視網膜節細胞的生理特性初探。在形態研究上是利用顯微注射 Neurobiotin 染劑的方式去評估節細胞樹突結構與連結模式。在電生理的實驗中，我們與交通大學吳重雨教授合作視網膜晶片計畫，記錄 SD 大鼠的節細胞對光刺激與電刺激的反應，也記錄 RCS 大鼠的節細胞對電刺激的反應，其中電刺激的來源是藉由雷射光去引發下視網膜感光二極體矽晶片所產生。雖然我們並沒有發現 RCS 大鼠的節細胞能對下視網膜晶片的電刺激產生反應，但在節細胞的形態方面，我們卻發現包括節細胞樹突的總長度、樹突分支點的數量、樹突節點的出現率以及染劑連通其他細胞的模式在重塑晚期的 RCS 大鼠中都相較於正常大鼠有顯著差異。這項發現顯示節細胞的形態在退化晚期的 RCS 大鼠中已經出現明顯改變，因此這項特性也說明在治療退化晚期色素性視網膜炎的策略上，不能夠假設殘存的視網膜節細胞其功能仍然完好。

關鍵字：視網膜重塑，色素性視網膜炎，樹突形態

ABSTRACT

The retinal remodeling is known in a human inherited disease, retinitis pigmentosa (RP), which leads to the loss of vision caused by photoreceptor degeneration. It has been reported in the Royal College of Surgeons (RCS) rat which is one of animal models for studying human retinitis pigmentosa that the degenerated photoreceptors cause a dramatic reorganization of retina, including the inner nuclear layer and the ganglion cell layer, at later stages in the RCS rat. At present treatments for restoring vision in RP founded on the intact properties of remaining neurons, and the remodeling of retinal degeneration at later stages were neglected. However, the morphological features of retinal ganglion cells (RGCs) in the RCS rat at later stages of degeneration have not been carefully studied. Therefore, the goals of this study were to characterize the properties of RGCs at later stages in morphology and electrophysiology. In the present study, we characterized morphological properties of RGCs in two aged groups of RCS rats (P331-418 and P526-575) and two strains of normal rats (SD and LE). In addition, examination of the physiological properties of RGCs in SD and RCS rats was also attempted. The responses of RGCs upon light and electrical stimulations in SD rats, and those upon electrical stimulation in RCS rats were recorded. Microinjection with Neurobiotin was used to assess the dendritic morphologies and coupling patterns of RGCs. In collaboration with Prof. CY Wu (National Chiao Tung University) in retinal prosthesis program, the electrical stimulation was provided by activating a silicone-based microphotodiode array with a 532 nm laser from the

subretinal side. Although we did not find RGC responses upon electrical stimulation in the RCS rat, the morphological features of RGCs, including total dendritic length, number of branching points, appearance of dendritic beads, and tracer coupling patterns in the RCS rats were significantly different from those in the normal rats. The finding indicates that RGCs in the RCS rat may undergo significant changes during the retinal remodeling at later stages of degeneration. This also suggests that the strategy of treating RP at later stages cannot assume intact RGCs.

Key words: retinal remodeling, retinitis pigmentosa, dendritic morphology