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炎症性サイトカインはCaco2細胞や濾胞関連上皮モデル細胞の排泄輸送系を亢進させる

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【Purpose】When the inflammatory reaction occurs in the human body, the well-known pro-inflammatory cytokines such as IL-1b, TNF-a, IL-6 and IL-4 are highly expressed at that site. We need to consider the possibility of their effect on the drug transporters. FAE-cells which are located in Peyel's patch have the function to capture the exogenous factors such as bacteria and viruses. If we use Caco2 cells and FAE-like cells, we can follow most of the intestinal cell lines under either normal conditions or inflammatory ones. In this study, we tried to evaluate the change in transport activity regarding efflux transporters, especially p-GP in these cells.

【Method】We used Caco2 cells, FAE-like cells[1)] and new FAE-like cells stimulated by cytokines in our transport study. Mannitol as the paracelluler marker, Cilostazol and Rerbamipide which have been marketed in Japan were used in this study as the model drugs. Cyclosporin was used as the p-GP inhibitor.

【Results & Discussion】In the FAE-like cells stimulated by IL-6, p-GP highly contributed to Cilostazol, which is also known as p-GP substrate, membrane transport. However, this wasn't observed in Caco2 and FAE cell models without stimulation by cytokines. This phenomenon was also observed in Caco2 cells stimulated by cytokines. Furthermore, at high doses of cytokines the improvement in p-GP condition wasn't observed. Taken together, cytokines must up-regulate the efflux transporters for at least p-GP and we have to pay attention to the cell viability if we hope high p-GP activity to be maintained.

【References】 1) Kernéis *S., Science*, 1997, 277, 949-952.