Mcl-1 蛋白之功能解析 -由找尋其交互作用之蛋白探討

Functional characterization of Mcl-1 by searching for Mcl-1 interacting proteins

中文摘要

Mcl-1 屬於 Bcl-2 家族蛋白質之一，而此家族成員多參與調控細胞凋亡的過程。Mcl-1 如同其他 Bcl-2 家族成員一樣，擁有相似的 BH1、BH2、BH3 以及膜鑲嵌區域。先前的研究指出，Mcl-1 是血癌細胞分化過程中引發的一個蛋白。最近也發現 Mcl-1 在 granulocyte macrophage colony-stimulating factor (GM-CSF) 及 interleukin 3 (IL-3) 所引發的細胞存活反應中扮演一重要角色。在一些研究中證明了不同抗細胞死亡及促進細胞死亡的 Bcl-2 相關蛋白質之間的交互作用對於決定細胞的命運上是十分關鍵性的的。例如當 Bax 與 Bcl-2 形成異構物 (heterodimer) 時便會中和 Bax 促進細胞凋亡的能力。相同的，Mcl-1 也會與一些 Bcl-2 家族成員形成異構物，如 Bok、Bax、Bak 及 Bik。在此篇研究中，我透過 Yeast two hybrid 方法來找尋 Mcl-1 在淋巴球中之交互作用蛋白，藉以了解 Mcl-1 在此系統中之功能。藉由篩選淋巴球 cDNA library，我發現了 58 個候選蛋白可能會與 Mcl-1 進行交互作用，其中包括了 Bcl-2 家族成員 Bax、Bid 及 Bik。我也發現了一些未被確定的人類基因，名為 KIAA0147，KIAA0719 以及 TPT1 亦會與 Mcl-1 進行交互作用。在試管內的 GST-pull down 研究中顯示 KIAA0719 及 TPT1 會與 Mcl-1 交互作用，但 KIAA0147 並不會。未來將進一步探討是否 Mcl-1 會與 KIAA0719 及 TPT1 在細胞內進行交互作用。

英文摘要

Mcl-1 belongs to the Bcl-2 protein family whose members participate in the regulation of apoptosis. It shares homologous BH1, BH2, BH3 and transmembrane domain with other Bcl-2 family members. Previous studies showed that Mcl-1 is induced during differentiation of leukemic cells. It was recently demonstrated that Mcl-1 is one of the survival components elicited by granulocyte macrophage colony-stimulating factor (GM-CSF) and interleukin 3 (IL-3). Some studies demonstrated that interaction between different anti- and pro-apoptotic Bcl-2 related proteins are critical in the determination of cell fate. For example, neutralization of pro-apoptotic activity of Bax occurred when it heterodimerized with Bcl-2. Mcl-1 also heterodimerized with some Bcl-2 family members like Bok, Bax, Bak and Bik. In this study, I analyzed Mcl-1 function in lymphocyte through searching for its interaction proteins by the yeast two hybrid system. By screening the human lymphocyte library, I found 58 candidates that may interact with Mcl-1, including Bax, Bid and Bik that belong to the Bcl-2 family. I also found some unidentified human genes named

KIAA0147, KIAA0719, and one tumor protein, named TPT1 (tumor protein, translationally-controlled 1), to interact with Mcl-1 in the yeast two hybrid system. In-vitro GST-pull down assay showed that KIAA0719 and TPT1 but not KIAA0147 interacted with Mcl-1. It remains to be determined whether Mcl-1 interacts with KIAA0719 or with TPT1 in-vivo.