

第97回生物科学フロンティアセミナー

“Saporin-based chimeric fusions as therapeutic option for the treatment of solid tumors”

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リボソーム不活化タンパク質であるサポリンは、低濃度で高い抗がん活性を有し、且つ血中での安定性が高いことから次世代のバイオ医薬品としての可能性が期待されています。本講演ではサポリンの基礎から細胞標的技術に関する最新の知見をお話し頂きます。

Abstract:

For decades, cancer therapy has been based on biophysical parameters, with surgical resection to debulk followed by radiation and chemotherapy to target the rapidly growing tumor cells. Nevertheless, the high rate of cancer recurrence, as well as the systemic toxicity of conventional treatments and the development of multidrug resistance support the need of advanced and personalized therapies. So far, toxins have shown promising results in preclinical studies. The type I ribosome-inactivating protein (RIP) saporin (SAP), in particular, has been extensively studied because of its stability, low immunogenicity, resistance to blood proteases and to conjugation procedures. In fact, due to the lack of a binding domain, it can be conjugated to specific targeting peptides, able to recognize and bind aberrant receptors overexpressed on the surface of cancer cells. In the current study, we have developed a toxin-based therapeutic approach, consisting in recombinant SAP-based chimeras, in order to selectively target tumor cells and tumor microenvironment. We demonstrated that the SAP-based chimeras impair cell viability in a dose-dependent manner, resulting in a selective cytotoxic activity on cancer cells expressing the target receptors. In contrast, SAP WT, do not exert any effect due to its lack of specificity. Moreover, the toxicity of chimeras is unambiguously due to the presence of SAP, as a catalytically inactive mutant do not enhance any antitumor effect. These data suggest that SAP based therapeutics represent a suitable option in oncological field to cope with cancer heterogeneity. The molecular characterization of a wider range of tumor cells will provide valuable information to extend their preclinical validation.

（本セミナーは大学院講義（細胞機能制御化学 特論）内で行われます）

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