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One-dimensional poly(L-lysine)-block-poly(L-threonine) assemblies as anticancer agents

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We synthesized cationic, one-dimensional fibril assemblies formed from coil-sheet poly(L-lysine)-block-poly(L-threonine) (PLL-b-PLT) block co-polypeptides as anticancer agents. The 1D fibril assemblies can efficiently interact with negatively charged cellular and mitochondrial membranes via electrostatic interactions, leading to cell necrosis through membrane lysis and apoptosis via the lytic effect of mitochondria. This effect is similar to that of one-dimensional drug carriers that exhibit enhanced cell penetration. Compared to free PLL chains, PLL-b-PLT fibril assemblies exhibited more selective cytotoxicity against cancer cells, lower hemolytic activity, higher membranolytic activity and a different apoptotic pathway, which may be due to differences in the peptide-membrane interactions. The fibril assemblies significantly inhibited tumor growth, improved survival and suppressed tumor metastasis to the lung in C57BL/6 mice bearing syngeneic LL2 lung tumors. An additive antitumor activity was also observed when the tumor bearing mice were treated with PLL-b-PLT in combination with the common chemotherapeutic drug cisplatin. Collectively, these results support the feasibility of using one-dimensional fibril assemblies as potential anticancer therapeutics.

Biography

Chao-Liang Wu is a Distinguished Professor of the Department of Biochemistry and Molecular Biology and Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Taiwan. He has received his PhD in Molecular Biology from University of Edinburgh. He has his expertise in the areas of translational medicine, animal models, gene therapy and nanotechnology. He has published more than 100 papers in peer-reviewed international journals.

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