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Alpha-fetoprotein complexes with toxins in fixing the cancer brakes

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The natural cancer brakes that serve the majority of us are apoptosis and the immune system. In cancer, both are broken. Apoptosis can be fixed by special toxins, and immune tolerance can be overcome with immunotherapy. Alpha-fetoprotein (AFP) is the delivery protein produced by the embryo. It crosses three layers of the human hemochorial placenta which separate the two circulations. In the blood, it binds polyunsaturated fatty acids (PUFAs) which the mother has to take by food as she does not produce them herself. AFP has a hydrophobic pocket that binds PUFAs stronger than blood proteins do. AFP delivers PUFAs to embryonic and myeloid-derived suppressor cells (MDSCs) through AFP receptor (AFPR)-mediated endocytosis like a shuttle. Meanwhile, MDSCs suppress embryo rejection by the mother's immune system.

MDSCs forms the protective tumor microenvironment (TME). As well as growing cancer cells, MDSCs can be hit by AFP-toxin preparations. The special toxins activate apoptosis in MDSCs and restore broken ones in cancer cells. MDSCs depletion by AFP-toxin preparations cancels the immune tolerance to tumors. MDSCs-targeted chemotherapy is a perspective cancer immunotherapy. Injectable AFP-toxin non-covalent complexes have demonstrated anticancer activity.

There has been a great desire for enabling the non-invasive delivery of therapeutics across mucosal surfaces. Oral porcine AFP complexes with toxins demonstrated anticancer activity, though they were not traced in the blood of mice. Gastrointestinal (GI) tract lymph nodes are lacking MDSCs and should have other sensitive immune-suppressive cells, which depletion eventually leads to distant metastases reduction. Hence, the cancer cells are not the only target for porcine AFP-toxin complexes, and immune suppressor cells "are more equal than others". The possible role of neonatal Fc receptor (FcRn) in transcytosis of oral porcine AFP complexes with toxins through intestinal enterocytes to GI tract lymph nodes is discussed.

Biography

Dr. Vladimir Nikolayevich Pak graduated from the Novosibirsk State University, received his Ph.D. from the Institute of Bioorganic Chemistry, Moscow, before working at the Novosibirsk Institute of Molecular Biology, Russia, and several biotechnological companies. He has over 35 years of experience in genetic engineering, virology, immunology, and biotechnology. His work focuses on the manufacturing of active pharmaceutical ingredients and the implementation of the drug candidates based on injectable (Reducin) and peroral (Aimpila) forms of AFP+toxin(s) non-covalent complexes. AFP+toxin non-covalent complexes, as well as AFP+toxin chemical conjugates, are likely to have both, direct cytotoxic effect on cancer cells and an immune checkpoint inhibition effect without toxicity. Dr. Vladimir N. Pak is the author of numerous scientific articles, patents, and a book.

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