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Geometry of ah receptor' ligand binding site studied with idiotypic and anti-idiotopic monoclonal antibodies to 2,3,7,8-tcdd.

Ilya B Tsyrlov
Icahn School of Medicine, USA

An original approach was developed consisting of the development of monoclonal antibodies (Mab) against the most potent xenobiotic 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The TCDD was adducted by the adipine fragment synthesized with the carrier protein. The Mab obtained allow to increase significantly a sensitivity of immunochemical quantitative analysis of TCDD amount in biological tissues, especially by using a time-resolved fluorimetry of the complex of the Mab with europium or another lanthanum element. That made possible to avoid very laborious and expensive HPLC/double mass spectrometry analysis of bio-concentrations of TCDD, which usually linked to TCDD ability to trans-activate key genes related to chronic inflammation and other toxic effects. The biological effects of TCDD can be defined strictly due to this ligand extremely strong binding to the its own Ah receptor, a mediator of all TCCD-activated transcriptional pathways. Therefore, the anti-ligand Mab obtained could be used for semi-quantitate assessment of TCDD-Ah receptor interactions (see the scheme). Selection of an antibody that binds to the idiotope outside the antigen binding site of the drug results in an antibody that can be used to detect both free and bound drug in the sample o Anti-idiotypic antibody o Detects total ligand (TCDD), free, partially bound, fully bound Moreover, the anti-TCDD Mab might serve a suitable immunogen to elicit anti-anti-ligand Mab via the idiotypic network. Whether the anti-idiotypic Mab binding to the Ah receptor to be completely inhibited by the ligand (TCDD), that might give an approach to more précised investigation of geometry and function of the Ah receptor binding site(s).

Biography

Ilya B. Tsyrlov is a professor at Icahn School of Medicine, USA. he has attended so many inetrnational conferences.

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