Homomeric and Heteromeric Interactions of the Extracellular Domains of Death Receptors and Death Decoy Receptors

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Death receptors (DRs) can induce apoptosis by oligomerization with TRAIL, whereas death decoy receptors (DcRs) cannot due to the lack of functional intracellular death domains.[1-4] However, it is not fully known yet whether DRs and DcRs can interact one another to form oligomeric complexes before TRAIL binding. To address this issue, the extracellular domains (ECDs) of DR4 (sDR4), DR5 (sDR5), DcR1 (sDcR1), and DcR2 (sDcR2) were expressed in a soluble, monomeric form in bacteria andtheir binding interactions were quantified by surface plasmon resonance measurements. The purified sDRs and sDcRs exhibited proper secondary structures and bound to TRAIL with nanomolar range affinity (K_D = ~10 - 62 nM), suggesting that they were properlyfolded and functional. The soluble receptors interacted homophilically and heterophilically with similar micromolar range affinity (K_D = ~1- 9 μM), except that sDR5 did not interact with sDcRs. Our results suggest that DRs and DcRs could laterally interact to form homomeric and/or heteromeric complexes through their ECDs on the cell surface, except for DR5-DcRs, even before TRAIL binding.

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