

Role and Potential Therapeutic Use of TRAIL in Diabetes

Ahter Dilşad Şanlıoğlu

Human Gene and Cell Therapy Center, Department of Medical Biology and Genetics, Faculty of Medicine,
Akdeniz University. Antalya, Turkey

TNF-related apoptosis-inducing ligand (TRAIL) is a TNF superfamily member, defined by its high homology to CD95L/FasL and TNF-alpha. It is known for its strong selective apoptotic effect on many transformed cell lines and tumor cells but not in most normal cell types. TRAIL appears to be a more complex molecule than predicted, with a higher therapeutic potential than previously anticipated. This is mainly because it has 5 different receptors that it can bind to in contrast to other TNF family members with one or two receptors; it is expressed widely in human tissues; and it has anti-inflammatory effects. For instance, type 1 diabetes (T1D) development was exacerbated in non-obese diabetic (NOD) mice when TRAIL function was blocked, and TRAIL^{-/-} C57BL/6 mice developed T1D at a much earlier stage following streptozotocin (STZ) injection, compared to mice which displayed normal TRAIL expression. Furthermore, TRAIL displayed a pro-angiogenic effect in primary human vascular endothelial cells. It also induced survival against the apoptosis triggered by pro-inflammatory cytokines in vascular smooth muscle cells, as well as promoting migration and proliferation. Results from studies aiming to clear out the role of TRAIL in diabetes development suggest a protective role for this molecule on beta cells. TRAIL generally does not induce beta cell apoptosis, plays a protective role in these cells against the apoptotic effects of cytokines such as FasL and TNF-alpha, and its receptors are expressed at a significant level in the pancreatic islets. While TRAIL's role or potential use in diabetes is investigated in various cell and animal systems by many research groups including ours, it is still not clearly identified. Our previous and current results, which mainly support a protective role for TRAIL, will be discussed comparatively with similar and contradictory results of other groups.
