

12th European Diabetes Congress

September 15-17, 2016 Berlin, Germany



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Cell surface CD44 of β cell, a mediator of β cell destruction in autoimmune diabetes

CD44 is a multi-functional receptor with multiple isoforms engaged in modulation of cell trafficking and transmission of apoptotic signals. We have previously shown that injection of anti-CD44 antibody into NOD mice induced resistance to type 1 diabetes (T1D). In this communication we describe the mechanism underlying this effect. We found that CD44-deficient NOD mice develop stronger resistance to T1D than wild-type littermates. This effect is not explained by the involvement of CD44 in cell migration, because CD44-deficient inflammatory cells surprisingly had greater invasive potential than the corresponding wild type cells, probably owing to molecular redundancy. We describe here a mechanism underlying the T1D enhancement that has not yet been previously reported. CD44 expression and hyaluronic acid (HA, the principal ligand for CD44) accumulation were detected in pancreatic islets of diabetic NOD mice, but not of non-diabetic DBA/1 mice. Expression of CD44 on insulin-secreting β cells renders them susceptible to autoimmune attack, leading to β cell apoptotic destruction as indicated by TUNEL assay as well as by functional assays exhibiting increased nitric oxide release, reduced insulin secretion after glucose stimulation and decreased insulin content in β cells. All these parameters could not be detected in CD44-deficient islets. We further suggest that HA-binding to CD44-expressing β cells is implicated in β -cell demise. Altogether, these data demonstrate that CD44 is a receptor capable of modulating cell fate. This finding is important for other pathologies (e.g., cancer, neurodegenerative diseases) in which CD44 and HA appears to be implicated.

Biography

David Naor is a Professor of Immunology in the Hebrew University, Faculty of Medicine and was the Head of Milton Winograd Chair of Cancer Studies. He received his PhD from the Hebrew University. He served as visiting Professor in leading universities (e.g., UCLA, Harvard). He published 152 articles, including in leading journals like *Nature*, *PNAS*, *J Clin Invest*, *J Immunol*, *J Exp. Med.* etc. His current research has been focused on the role of CD44 and other hyaluronan-binding molecules (e.g., RHAMM) in autoimmune and cancer diseases. This CD44 research yielded 34 articles, which were cited thousands of times. He was invited to speak on CD44 at 8 plenary sessions of international conferences. He has been a Member in Editorial Boards of several international scientific journals and he is on the scientific board of International Congress on Autoimmunity. He received awards from Johnson & Johnson "In recognition of outstanding research towards the advances of science and technology in health care" and from the Hebrew University for his "outstanding achievements in research and teaching."

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