>11.3% (100 mmol/mol) at presentation. Key findings: 1) A small proportion of people with T1D, negative for GADA, IA-2A and ZnT8A, were Tspan7A positive. 2) Younger age at diagnosis and pancreatic autoantibody positivity were independent predictors of Tspan7A positivity. 3) The characteristics of those positive only for Tspan7A were diverse.
Conclusion: Tspan7A positivity is associated with a younger age at diagnosis in T1D. 4.6% of autoantibody negative individuals were positive for Tspan7A and, though small in number, these individuals had variable clinical characteristics. Younger individuals who are negative for GADA, IA2A and ZnT8A, may benefit from additional measurement of Tspan7A. Larger studies are needed to examine further the characteristics of these individuals.
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Mechanotransduction in human and mouse beta cell lines: reliable models to characterise novel signalling pathways controlling beta cell fate

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Background and aims: Attempts to influence β-cell differentiation by engineering substrates that mimic appropriate extracellular matrix (ECM) topographies are hampered by the fact that profound details of mechanosensing/transduction complexity remain elusive. We recently demonstrated that human islets of Langerhans sense the ECM nanotopography and activate a mechanotransductive pathway, which is essential for preserving long-term β-cell differentiation and function in vitro. However, human islets of Langerhans are extremely heterogeneous and their availability for research purpose is limited. Therefore, aim of the proposed research was to investigate whether mouse and human β-cell lines might sense changes in the ECM topography and might be used as a simplified model to dissect the molecular pathways involved in mechanotransduction.
Materials and methods: We used supersonic cluster beam deposition to fabricate nanostructured substrates characterized by a quantitatively controllable ECM-like nanoroughness. Mouse βTC3 and human 1.1B4 cells were seeded on these substrates and after five days in culture, the activation of the mechanotransductive pathway was verified by means of morphological (super-resolution fluorescence microscopy), functional and proteomic techniques.
Results: Quantitative immunofluorescence studies demonstrated that the cell-nanotopography interaction affects the focal adhesion structures (smaller vinculin clusters), the organization of the actin cytoskeleton (shorter actin fiber) and the nuclear architecture. Functional studies revealed that nanostructured surfaces improve the β-cell mitochondrial activity and increase the glucose-stimulated Ca^{2+}currents and insulin release. Label-free shotgun proteomics broadly confirmed the morphological and functional studies and showed the upregulation of a number of mechanosensors and transcription factors involved in β-cell differentiation in cells grown on nanostructured substrates compared to those grown on flat standard control surfaces.
Conclusion: Our data reveal that mouse and human β-cell lines sense changes in extracellular mechanical forces and activate a mechanotransductive pathway. The findings from this study will be useful to clarify the link between mechanotransduction and cell fate and to successfully engineer scaffolds in order to have functional beta cells.
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The long non-coding RNA PAX6-AS1 controls human beta cell identity

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Background and aims: Long non-coding RNAs are crucial components of the pancreatic islet regulome whose mis-expression may contribute to