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Differentiation – P35

The role of AMP Kinase on the beta-cell differentiation of mouse embryonic stem cells.
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Background:

Beta-cell differentiation from embryonic stem cells involves complex signaling mechanisms. Nutritional status of the mother was shown to have a profound effect on offspring’s beta-cell numbers, islet cell size, proliferation capacity and islet-insulin content. This prompted us to investigate the role of whole-body energy sensor AMP Kinase on the expression of pancreas specific transcription factors and on beta-cell differentiation of mouse embryonic stem cells.

Materials and methods:

CGR8 mouse embryonic stem cells were used for this study. Chemical activators and inhibitors were used for modulating the AMP Kinase signaling in differentiating embryonic stem cells. RT-PCR experiments were used for monitoring the mRNA expression of several pancreas specific transcription factors (Hnf-6, Mac A, Neutrogena 3, Neuron D1, Foxa2, Pdx-1) during the course of embryonic stem cell differentiation, in the presence and absence of AMP Kinase activators and inhibitors. The relationship between TGF-beta signaling pathway and AMP Kinase signaling was studied using RT-PCR and western blot.

Results:

The results showed that modulating AMP Kinase signaling pathway of mouse embryonic stem cells has a profound influence on the expression of pancreas specific transcription factors. Inhibition of AMP Kinase during the earlier stages of embryonic stem cell differentiation increases the fold expression of pancreas specific transcription factors while activation of AMP Kinase has an opposite effect. Experiments with AMP Kinase activators show that TGF-beta mRNA expression was down-regulated by metformin, an AMP Kinase activator.

Conclusion:

Initial experiments showed that AMP Kinase signaling pathway has a strong effect on the expression of pancreas specific transcription factors in mouse embryonic stem cells. Studying the relationship between AMP Kinase and TGF-beta pathway will help in understanding the interplay of these signaling molecules in the beta-cell differentiation of embryonic stem cells.