



CDB SEMINAR

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13:30~15:00 C1F CDB Auditorium



Krüppel-like factors: Key molecular regulators of cardiovascular biology

Summary

Krüppel-like factors (KLFs) are a subclass of the zinc-finger family of transcriptional regulators implicated in the regulation of cellular growth and differentiation and tissue development. The term Krüppel is a german word meaning "cripple." This is based on the observation that Drosophila embryos homozygous for Krüppel die due to altered thoracic and anterior abdominal segments. Over the past 13 years, 17 mammalian KLFs have been identified and found to play important roles in diverse cell types. Accumulating evidence implicates members of this family as key regulators of gene expression and function in diverse biological processes critical to the cardiovascular system, stem cell biology, cancer development, and metabolism. Studies from our laboratory have evaluated the role of this family of factors in endothelial, immune cell, and muscle biology.

(1) Muscle – We identified KLF15 as being expressed in adult cardiomyocytes and vascular smooth muscle cells in vitro and in vivo. KLF15 is a regulator of cardiac and smooth myocyte in response to stress such as pressure overlord. The development of novel approaches aimed at regulating KLF15 expression or function may provide a foundation for novel therapeutic approaches in the treatment of cardiovascular disease.

(2) Endothelial – The expression of KLF2 and KLF4 are both robustly induced by laminar flow. In contrast KLF2 expression is reduced by pro-inflammatory stimuli while that of KLF4 is induced. Overexpression of KLF2 and KLF4 induces laminar flow induced targets such as endothelial nitric oxide synthase and thrombomodulin – two key factors that confer anti-adhesive, anti-thrombotic properties to the endothelium. , these observations identify KLF2 & KLF4 as overlapping factors that serve as ‘molecular switches’ regulating key aspects of endothelial homeostasis.

Host:

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