

综述

利用功能基因组学方法研究SMAD去磷酸化—TGF- β 超家族信号转导的终止机制

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摘要

在后生动物机体中, 转化生长因子 β (TGF- β)及相关生长因子可以通过自分泌、旁分泌及内分泌方式影响广泛的生理活动。它们在多种疾病的发病过程中起着重要的作用, 尤其是癌症、纤维化疾病、自免疫疾病和心血管系统疾病。TGF- β 受体介导的R-SMADs的磷酸化是TGF- β 信号转导通路中最重要的步骤, 引起从细胞质内SMAD复合体的组装到核内转录调控这样一个细胞内的信号转导。因此, R-SMADs的去磷酸化是TGF- β 信号转导终止的一个重要机制。最近, 我们实验室结合功能基因组学、生物化学和发育生物学的方法, 鉴定并研究了磷酸酶PPM1在TGF- β 信号转导调控中的功能。文章简短地总结了SMADs动态的磷酸化和去磷酸化是如何调控信号转导的强度和持久性以及TGF- β 信号转导的生理功能。

关键词 [转化生长因子\(TGF- \$\beta\$ \); SMADs; 去磷酸化](#)

分类号

Termination of TGF-beta Superfamily Signaling Through SMAD Dephosphorylation—A Functional Genomic View

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Abstract

The transforming growth factor- β (TGF- β) and related growth factors activate a broad range of cellular responses in metazoan organisms via autocrine, paracrine, and endocrine modes. They play key roles in the pathogenesis of many diseases especially cancer, fibrotic diseases, autoimmune diseases and cardiovascular diseases. TGF- β receptor-mediated phosphorylation of R-SMADs represents the most critical step in the TGF- β signaling pathways that triggers a cascade of intracellular events from SMAD complex assembly in the cytoplasm to transcriptional control in the nucleus. Conversely, dephosphorylation of R-SMADs is a key mechanism for terminating TGF- β signaling. Our labs have recently taken an integrated approach combining functional genomics, biochemistry and development biology to describe the isolation and functional characterization of protein phosphatase PPM1A in controlling TGF- β signaling. This article briefly reviews how dynamic phosphorylation and dephosphorylation of SMADs control or fine-tune the signaling strength and duration and ultimately the physiological consequences in TGF- β signaling.

Key words [transforming growth factor- \$\beta\$ \(TGF- \$\beta\$ \); SMADs; dephosphorylation](#)

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