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Recent Progress of Plant Apoptosis. YANG Zheng, CAI Chen-Leng, SONG Yun-Chun (*College of Life Sciences, Wuhan University, Wuhan* 430072, China).

Abstract　Apoptosis is an active programmed cell death process during the organism development, cell differentiation and pathological situation. Many studies have revealed that apoptosis is an important and normal part in plant embryo development, tracheary element formation and development of root, shoot, leaf, flower. In hypersensitive response, plants use apoptosis in response to infection by pathogens to protect the whole plant survival.

Key words　apoptosis, plant, development, hypersensitive response

转化生长因子β受体的研究进展

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摘要　转化生长因子β受体为胞膜蛋白, 存在5种形态, Ⅲ型受体主要是调节受体与配体之间的亲和力及Ⅱ型受体的膜上表达. 功能性受体则主要为Ⅰ、Ⅱ型. Ⅰ、Ⅱ型受体在介导信号传递时相互配合, 又存在分工不同: Ⅰ型受体为介导转化生长因子β促细胞外基质合成的信号通道. 而Ⅱ型受体则与细胞的增殖、分化密切相关.

关键词　转化生长因子β受体, 信号传递, 生物作用

学科分类号　R318

转化生长因子β (TGF-β) 是近年来发现的一个重要的生长因子家族, 其生物学活性非常广泛, 参与体内形态发生、组织发育、免疫反应、造血及纤维化等过程. 而负责介导其信号传递的受体目前日益受到重视. 现已发现TGF-β受体 (TβR) 存在5种形态, 分别为TβR-Ⅰ、Ⅱ、Ⅲ、Ⅳ、Ⅴ. 其中TβR-Ⅳ及TβR-Ⅴ仅分别在垂体细胞和牛肝中发现. 目前研究得较多的是前三种受体. 几乎所有

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体细胞均表达两种或两种以上的 TβR，其中以 TβR-Ⅲ含量最丰富，每个细胞中约 2×10^5，为与 TGF-β 结合的主要受体.

1　TβR 的结构

TβR 均为胞膜蛋白，包括 3 个组成部分：富含半胱氨酸的胞外区、跨膜区及胞内区. TβR-Ⅰ与 TβR-Ⅱ在结构上非常相似：均为糖蛋白；有一较短的胞外区及一富含丝氨酸/苏氨酸的蛋白激酶的胞内区. 但两种受体的蛋白激酶区只有 41% 的氨基酸同源. 另外在两种受体的 C 端，TβR-Ⅰ有一较短的含 5 个氨基酸的残基，而 TβR-Ⅱ的则较长，由 24 个氨基酸组成. 再者，在 TβR-Ⅰ的蛋白激酶区的前端近胞膜处有一 GC 区，为 TβR-Ⅰ的核心系列：SGSGSG (富含丝氨酸及甘氨酸)，此结构在 TβR-Ⅰ中高度保守，而 TβR-Ⅱ则无此结构[1]. TβR-Ⅲ又称 β-聚糖，其胞外区相对较长，而胞内区却很短，只有 41 个氨基酸组成，没有明显的信号修饰装置，不直接参与信号传递[2].

2　生物学作用

由于 TβR-Ⅰ、TβR-Ⅱ、TβR-Ⅲ结构上的差异，其功能亦存在不同. TβR-Ⅲ胞外区较长，但无胞内信号修饰装置，故不直接参与信号传递. 其功能主要是调节受体与配体之间的亲和力及 TβR-Ⅱ的膜上表达. 它与 TGF-β_1，β_2，β_3 的亲和力相近，为 TGF-β 的主要结合形式[2].

TβR-Ⅰ、Ⅱ为功能性的受体，介导几乎所有的 TGF-β 的功能. 它们与 TGF-β_1 的亲和力要比与 TGF-β_2 的亲和力大 10~80 倍. 虽然两者在介导信号传递时的具体作用机制目前还不太清楚，但有资料表明两者在信号传递中密切配合：TβR-Ⅰ必须依赖 TβR-Ⅱ的存在方能与配体结合，而 TβR-Ⅱ必须依赖 TβR-Ⅰ参与方能完成信号传递过程. 其作用模式为：配体先与 TβR-Ⅱ结合，TβR-Ⅱ自身磷酸化 (磷酸化部位在 C 端 Ser549，Ser551 及近膜区的 Ser223，Ser226，Ser227)，紧接着 TβR-Ⅰ相互聚积成复合体或与 TβR-Ⅱ结合呈嵌合态，然后 TβR-Ⅰ的蛋白激酶磷酸化 (磷酸化部位为近膜区 GS 区：Thr185，Thr186，Ser187，Ser189，Ser191 及 N 端 Ser165)，再将信号传递到下游物质[3]，完成信号传递.

另外，TβR-Ⅰ与 TβR-Ⅱ又存在分工的不同. Chen[4] 曾将突变型的 TβR-Ⅱ (此突变型的 TβR-Ⅱ无胞内部分，而跨膜部分及胞外部分均无改变) 转染到 QT6 细胞株中 (此细胞株无 TβR-Ⅱ的表达，但有 TβR-Ⅰ的表达). 发现此转染的细胞株对 TGF-β_1 抗上皮细胞增殖作用及对 pRB 的去磷酸化作用被阻断，而 fibronectin 的合成不受影响；Takeuchi[5] 在观察 4 种骨髓瘤细胞株对 TGF-β_1 的反应时亦发现了非常有趣的现象：4 种骨髓瘤细胞株分别为 MC3T3-E1、MG63、SeOS2、UMR106，前两株细胞有 TβR-Ⅱ及 TβR-Ⅰ的正常表达，第三株细胞表达正常量的 TβR-Ⅰ，但 TβR-Ⅱ表达很少，第四株细胞则无 TβR-Ⅱ及 TβR-Ⅰ的表达. 将这 4 株骨髓瘤细胞与 TGF-β_1 共同孵育后，结果发现：TGF-β_1 既可抑制 MC3T3-E1 及 MG63 的增殖，又可刺激其合成 decorin 及 fibronectin 增加；但对其增殖无抑制作用；而 UMR106 对 TGF-β_1 则无反应. 也就是说，凡是有 TβR-Ⅰ表达的骨髓瘤细胞株，TGF-β_1 可刺激其合成细胞外基质增加，而凡是有 TβR-Ⅱ表达的骨髓瘤细胞株，TGF-β_1 则可抑制其增殖. 这些研究结果均说明 TGF-β 受体在介导信号传递过程中至少存在两条或两条以上的通道，并强烈提示 TβR-Ⅰ与细胞外基质的合成有关，而 TβR-Ⅱ则与细胞增殖有关. 这为我们进一步了解肿瘤及纤维化的发病机理时提供了理论根据，也为抗肿瘤及抗纤维化的治疗提供了一可能的途径. 如在很多肿瘤细胞株中发现无 TβR-Ⅱ的表达[6]，但如将 TβR-Ⅱ基因转染到这些细胞株后，就能逆转这些细胞的成瘤性[7].

3　TβR 的调节

机体可根据不同的需要对 TβR 的表达水平进行调节. 如在肝部分切除后，TβR-Ⅰ、Ⅱ、Ⅲ mRNA 及蛋白质水平均迅速下降，24 h 达最低点，此时肝细胞 DNA 合成达高峰[8]. 又如在伤口愈合过程中，除 TGF-β 表达增加外，TβR-Ⅰ、Ⅱ的表达亦显著增加，这样有利于伤口的愈合[9]. 机体对 TβR 表达调节的作用机制目前还不太清楚，但有一点可以肯定的是与 TGF-β 有关. 虽说 TGF-β_1 对 TβR 表达的影响各家报道不一，但大多认为 TGF-β_1 对 TβR-Ⅰ的表达起上调作用，而对 TβR-Ⅱ的表面则起下调作用. 如 Brain 报道 TGF-β_1 可使 TβR-Ⅰ mRNA 的表达增加 3 倍[10]. Mackay[11] 报道当肠癌细胞与 TGF-β_1 共同孵化后，细胞内的 TβR-Ⅱ的表达稍增加，而 TβR-Ⅰ的表达则增加 2 倍. 但 Woodward 报道将上皮细胞株 MAC-T 与

50 pmol/ L的 TGF-β_1 共同孵化后，细胞内的 TβR 表达明显下降[12].

通过了解 TβR 的生物学功能，不仅有助于我们进一步了解 TGF-β 的作用机理，更为临床应用：如抗肿瘤治疗，抗纤维化治疗提供参考依据.

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Study of Tranforming Growth Factor β Receptor.
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Abstract Tranforming growth factor β receptor, divided into five types, are membrane protein. The functin of type Ⅲ receptor is regulating the affinity between receptor and ligand as well as the expression of type Ⅱ receptor. Type Ⅰ and type Ⅱ receptor are functional receptors. They cooperate closely while the signal transduction, and on the other hand. They function differently: type Ⅰ receptor acts as the signal pathway by which transforming growth factor β stimulate the increasing synthesis of extracellular matrix; type Ⅱ receptor has closely relationship to the proliferate and differentiate cells.

Key words transforming growth factor β receptor, signal transduction, biological function