

## Lck和Fyn对T细胞发育过程的影响

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**摘要** 胸腺中T细胞的发育及次级淋巴组织中成熟T细胞的活化均需要细胞能够对环境信号分子做出适应性的反应。在共刺激分子及细胞因子受体介导的信号参与下通过TCR(T cell receptor)及其辅助受体CD4和CD8与MHC/抗原肽复合物相互作用,可以诱导TCR信号通路激活并最终导致T细胞免疫反应的发生。Src家族激酶Lck(Lymphocyte-specific protein tyrosine kinase)和Fyn(Proto-oncogene tyrosine-protein kinase)的激活是启动TCR信号通路的关键因素。在T细胞的发育、阳性选择、初始T细胞的外周存活及由淋巴细胞缺失诱导的细胞增殖中都起着关键性的作用。研究显示,虽然这两种信号分子紧密相关,但在某些条件下Lck发挥着比Fyn更重要的作用,并且Fyn仅可以补充Lck的部分功能。文章针对这两个激酶在T细胞发育的整个过程中的作用机制进行了论述。

**关键词:** Lck Fyn TCR 细胞发育 信号转导

**Abstract:** The development of T cell in the thymus and the activation of mature T cells in the secondary lymphoid tissues require T cell to make adaptive responses to signaling molecules of environment. The activation of T cell receptor (TCR) signaling pathway could be induced by the interaction of the TCR and its co-receptor CD4 and CD8 with MHC/peptide complex. This process involves co-stimulatory molecules and signals mediated by cytokine receptors, which eventually leads to the occurrence of T cell immune response. The Src-family kinases lymphocyte-specific protein tyrosine kinase (Lck) and proto-oncogene tyrosine-protein kinase (Fyn) are expressed in T cells and serve as the signaling molecules that are activated downstream of TCR. These signaling molecules play key roles in development, positive selection, and peripheral maintenance of naive T cells and lymphopenia-induced proliferation of peripheral T cells. Both Lck and Fyn are required for each of these TCR-based signaling pathways, and Lck seems to be the major contributor, while Fyn can only supplement some functions of Lck. In this review, we discussed the mechanisms by which these two proteins perform functions in T cell development based on our current understanding.

**Keywords:** Lck, Fyn, TCR, cell development, signal transduction

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[1] Parsons SJ, Parsons JT. Src family kinases, key regulators of signal transduction. *Oncogene*, 2004, 23(48): 7906-7909. 

[2] Shortman K, Wu L. Early T lymphocyte progenitors. *Annu Rev Immunol*, 1996, 14(1): 29-47. 

[3] Sebzda E, Mariathasan S, Ohteki T, Jones R, Bachmann MF, Ohashi PS. Selection of the T cell repertoire. *Annu Rev Immunol*, 1999, 17(1): 829-874. 



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- [4] Palacios EH, Weiss A. Function of the Src-family kinases, Lck and Fyn, in T-cell development and activation. *Oncogene*, 2004, 23(48): 7990-8000. [crossref](#)
- [5] Kruisbeek AM, Haks MC, Carleton M, Wiest DL, Michie AM, Zúñiga-Pflücker JC. Branching out to gain control: how the pre-TCR is linked to multiple functions. *Immunol Today*, 2000, 21(12): 637-644. [crossref](#)
- [6] Wallace VA, Penninger J, Mak TW. CD4, CD8 and tyro-sine kinases in thymic selection. *Curr Opin Immu-nol*, 1993, 5(2): 235-240. [crossref](#)
- [7] Molina TJ, Perrot JY, Penninger J, Ramos A, Audouin J, Briand P, Mak TW, Diebold J. Differential requirement for p56<sup>lck</sup> in fetal and adult thymopoiesis. *J Immunol*, 1998, 160(8): 3828-3834.
- [8] Molina TJ, Kishihara K, Siderovski DP, van Ewijk W, Narendran A, Timms E, Wakeham A, Paige CJ, Hartmann KU, Veillette A, Davidson D, Mak TW. Profound block in thymocyte development in mice lacking p56<sup>lck</sup>. *Nature*, 1992, 357(6374): 161-164.
- [9] Appleby MW, Gross JA, Cooke MP, Levin SD, Qian X, Perlmutter RM. Defective T cell receptor signaling in mice lacking the thymic isoform of p59<sup>fyn</sup>. *Cell*, 1992, 70(5): 751-763.
- [10] Stein PL, Lee HM, Rich S, Soriano P. pp59<sup>fyn</sup> mutant mice display differential signaling in thymocytes and peripheral T cells. *Cell*, 1992, 70(5): 741-750.
- [11] Groves T, Smiley P, Cooke MP, Forbush K, Perlmutter RM, Guidos CJ. Fyn can partially substitute for Lck in T lym-phocyte development. *Immunity*, 1996, 5(5): 417-428. [crossref](#)
- [12] van Oers NSC, Lowin-Kropf B, Finlay D, Connolly K, Weiss A.  $\alpha\beta$  T cell development is abolished in mice lack-ing both Lck and Fyn protein tyrosine kinases. *Immunity*, 1996, 5(5): 429-436. [crossref](#)
- [13] Chu DH, van Oers NSC, Malissen M, Harris J, Elder M, Weiss A. Pre-T cell receptor signals are responsible for the down-regulation of Syk protein tyrosine kinase expression. *J Immunol*, 1999, 163(5): 2610-2620.
- [14] Levelt CN, Eichmann K. Receptors and signals in early thymic selection. *Immunity*, 1995, 3(6): 667-672. [crossref](#)
- [15] Zhang WG, Sommers CL, Burshtyn DN, Stebbins CC, DeJarnette JB, Triple RP, Grinberg A, Tsay HC, Jacobs HM, Kessler CM, Long EO, Love PE, Samelson LE. Es-sential role of LAT in T cell development. *Immunity*, 1999, 10(3): 323-332. [crossref](#)
- [16] Pivniouk V, Tsitsikov E, Swinton P, Rathbun G, Alt FW, Geha RS. Impaired viability and profound block in thy-mocyte development in mice lacking the adaptor protein SLP-76. *Cell*, 1998, 94(2): 229-238.
- [17] Abraham KM, Levin SD, Marth JD, Forbush KA, Perlmutter RM. Delayed thymocyte development induced by augmented expression of p56<sup>lck</sup>. *J Exp Med*, 1991, 173(6): 1421-1432. [crossref](#)
- [18] Anderson SJ, Abraham KM, Nakayama T, Singer A, Perlmutter RM. Inhibition of T-cell receptor  $\beta$ -chain gene rearrangement by overexpression of the non-receptor protein tyrosine kinase p56<sup>lck</sup>. *EMBO J*, 1992, 11(13): 4877-4886.
- [19] Levin SD, Anderson SJ, Forbush KA, Perlmutter RM. A dominant-negative transgene defines a role for p56<sup>lck</sup> in thymopoiesis. *EMBO J*, 1993, 12(4): 1671-1680.
- [20] Cooke MP, Abraham KM, Forbush KA, Perlmutter RM. Regulation of T cell receptor signaling by a *src* family protein-tyrosine kinase (p59<sup>fyn</sup>). *Cell*, 1991, 65(2): 281-291.
- [21] Salmond RJ, Filby A, Qureshi I, Caserta S, Zamoyska R. T-cell receptor proximal signaling via the Src-family kinases, Lck and Fyn, influences T-cell activation, differ-entiation, and tolerance. *Immunol Rev*, 2009, 228(1): 9-22. [crossref](#)
- [22] Hernández-Hoyos G, Sohn SJ, Rothenberg EV, Alber-ola-Ila J. Lck activity controls CD4/CD8 T cell lineage commitment. *Immunity*, 2000, 12(3): 313-322. [crossref](#)
- [23] Legname G, Seddon B, Lovatt M, Tomlinson P, Sarner N, Tolaini M, Williams K, Norton T, Kioussis D, Zamoyska R. Inducible expression of a p56<sup>lck</sup> transgene reveals a central role for Lck in the differentiation of CD4 SP thymocytes. *Immunity*, 2000, 12(5): 537-546. [crossref](#)
- [24] Olszowy MW, Leuchtmann PL, Veillette A, Shaw AS. Comparison of p56<sup>lck</sup> and p59<sup>fyn</sup> protein expression in thymocyte subsets, peripheral T cells, NK cells, and lymphoid cell lines. *J Immunol*, 1995, 155(9): 4236-4240.
- [25] Schmedt C, Saijo K, Niidome T, Kühn R, Aizawa S, Ta-rakhovsky A. Csk controls antigen receptor-mediated de-velopment and selection of T-lineage cells. *Nature*, 1998, 394(6696): 901-904.
- [26] Schmedt C, Tarakhovsky A. Autonomous maturation of  $\alpha\beta$  T lineage cells in the absence of COOH-terminal Src kinase (Csk). *J Exp Med*, 2001, 193(7): 815-826. [crossref](#)
- [27] Lovatt M, Filby A, Parravicini V, Werlen G, Palmer E, Zamoyska R. Lck regulates the threshold of activation in primary T cells, while both Lck and Fyn contribute to the magnitude of the extracellular signal-related kinase re-sponse. *Mol Cell Biol*, 2006, 26(22): 8655-8665. [crossref](#)
- [28] Zamoyska R, Basson A, Filby A, Legname G, Lovatt M, Seddon B. The influence of the src-family kinases, Lck and Fyn, on T cell differentiation, survival and activation. *Immunol Rev*, 2003, 191(1): 107-118. [crossref](#)
- [29] Seddon B, Legname G, Tomlinson P, Zamoyska R. Long- term survival but impaired homeostatic proliferation of Naive T cells in the absence of p56<sup>lck</sup>. *Science*, 2000, 290(5489): 127-131.
- [30] Seddon B, Zamoyska R. TCR and IL-7 receptor signals can operate independently or synergize to promote lym-phopenia-induced expansion of naive T cells. *J Immu-nol*, 2002, 169(7): 3752-3759.
- [31] Seddon B, Zamoyska R. TCR signals mediated by Src family kinases are essential for the survival of naive T cells. *J Immunol*, 2002, 169(6):

- [32] Jameson SC. Maintaining the norm: T-cell homeostasis. *Nat Rev Immunol*, 2002, 2(8): 547-556.
- [33] Filby A, Seddon B, Kleczkowska J, Salmond R, Tomlinson P, Smida M, Lindquist JA, Schraven B, Zamoyska R. Fyn regulates the duration of TCR engagement needed for commitment to effector function. *J Immunol*, 2007, 179(7): 4635-4644.
- [34] Gett AV, Sallusto F, Lanzavecchia A, Geginat J. T cell fitness determined by signal strength. *Nat Immunol*, 2003, 4(4): 355-360. 
- [35] Lanzavecchia A, Sallusto F. Progressive differentiation and selection of the fittest in the immune response. *Nat Rev Immunol*, 2002, 2(12): 982-987. 
- [36] Kim RK, Yoon CH, Hyun KH, Lee H, An S, Park MJ, Kim MJ, Lee SJ. Role of lymphocyte-specific protein tyrosine kinase (LCK) in the expansion of glioma-initiating cells by fractionated radiation. *Biochem Biophys Res Commun*, 2010, 402(4): 631-636. 
- [37] Scales TM, Derkinderen P, Leung KY, Byers HL, Ward MA, Price C, Bird IN, Perera T, Kellie S, Williamson R, Anderton BH, Reynolds CH. Tyrosine phosphorylation of tau by the SRC family kinases Ick and fyn. *Mol Neurodegener*, 2011, 6(1): 12. 
- [38] Lee KC, Ouwehand I, Giannini AL, Thomas NS, Dibb NJ, Bijlmakers MJ. Lck is a key target of imatinib and dasatinib in T-cell activation. *Leukemia*, 2010, 24(4): 896-900.
- [39] Schade AE, Gonzalez-Stawinski G. Immunomodulation via targeted inhibition of antigen receptor signal transduction. *Cardiovasc Hematol Disord Drug Targets*, 2008, 8(1): 1-6. 
- [1] 郑仲仲 沈金秋 潘伟槐 潘建伟.植物钙感受器及其介导的逆境信号途径[J]. 遗传, 2013,35(7): 875-884
- [2] 胡帅, 王芳展, 刘振宁, 刘亚培, 余小林.PYR/PYL/RCAR蛋白介导植物ABA的信号转导[J]. 遗传, 2012,34(5): 560-572
- [3] 程曦, 田彩娟, 李爱宁, 邱金龙.植物与病原微生物互作分子基础的研究进展[J]. 遗传, 2012,34(2): 134-144
- [4] 刘振华, 于延冲, 向凤宁.生长素响应因子与植物的生长发育[J]. 遗传, 2011,33(12): 1335-1346
- [5] 顾娟, 陈晓萍.神经发育中的细胞周期时程[J]. 遗传, 2011,33(11): 1185-1190
- [6] 马仙珏, 薛雷.双亮氨酸拉链激酶DLK对JNK信号通路的调控作用及机制[J]. 遗传, 2010,32(8): 785-790
- [7] 黄剑, 沈海龙, 刘长莉, 李玉花.植物不定芽离体再生分子调控的评述[J]. 遗传, 2007,29(5): 528-528-536
- [8] 王荣, 崔百明, 彭明, 张根发.赤霉素信号转导与棉纤维的分子发育[J]. 遗传, 2007,29(3): 276-276-282
- [9] 吴易阳 李岭.MicroRNA与肿瘤相关的信号转导通路[J]. 遗传, 2007,29(12): 1419-1428
- [10] 孙一明, 杨 涛, 许执恒.JNK 信号转导通路与神经迁移[J]. 遗传, 2007,34(11): 957-965
- [11] 蓝兴国, 于晓敏, 李玉花.配子体自交不亲和和信号转导的研究进展[J]. 遗传, 2005,27(4): 677-685
- [12] 元小红, 张 勤, 刘培琼, 宋春云, 徐如海.仔猪腹泻抗性相关特异表达ESTs的筛选[J]. 遗传, 2004,31(3): 251-256
- [13] 汪小凡, 陈家宽.野慈姑自然群体异交率的定量估测[J]. 遗传, 2000,22(5): 316-318