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综述

FANCL在原始生殖细胞的形成和范可尼贫血中的功能研究

赵庆国, 卢柏松, 黄培堂

北京生物工程研究所，北京 100071

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摘要 Fanconi氏贫血是一种罕见的常染色体隐性遗传性疾病，表现为进行性骨髓衰竭、先天性骨骼畸形和易患癌症等。FA病人细胞染色体自发不稳定，并对DNA交联剂如丝裂霉素C高度敏感。目前已发现11种FA蛋白参与形成了一种DNA损伤应答途径。新蛋白FANCL是FA复合物蛋白，作为E3连接酶催化FANCD2单一泛素化，泛素化FANCD2导向染色质与BRCA2相互作用，修复DNA损伤。FANCL、FANCC和FANCA等FA蛋白缺失造成生殖细胞缺失性不育，胚胎期生殖细胞中FA途径可能调控原始生殖细胞的增殖。FANCL和睾丸特异性蛋白质GGNBP1、GGNBP2以及OAZ3都与睾丸特异性蛋白质GGN1相互作用，形成睾丸特异性复合物，有可能在成年睾丸中影响精子生成。

关键词 FANCL；生殖细胞；Fanconi氏贫血

分类号

Functions of FANCL in Primordial Germ Cell Formation and Fanconi Anemia

ZHAO Qing-Guo, LU Bai-Song, HUANG Pei-Tang

Beijing Institute of Biotechnology, Beijing 100071, China

Abstract

Fanconi anemia(FA) is a rare autosomal recessive disorder characterized clinically by congenital abnormalities, progressive bone marrow failure and cancer susceptibility. Cells from individuals with Fanconi anemia manifest features of spontaneous chromosomal instability and hypersensitivity to DNA cross-linking agents such as mitomycin C. Over 11 known Fanconi anemia gene products are involved in DNA damage response pathway. In the pathway, monoubiquitination of FANCD2 is a key step. A novel protein FANCL is a component of the nuclear FA complex, functioned as an ubiquitin E3 ligase and monoubiquitinylated FANCD2. FANCD2-Ub is targeted to chromatin, where it interacts with BRCA2 to repair DNA damage. In early embryo stage, FA pathway is probably involved in proliferation of PGCs. Mice deficient in FA proteins, such as FANCL, FANCC and FANCA, have a drastic reduction of primordial germ cells(PGC), resulting in male and female infertility in adult. In the adult male, FANCL and a few testis-specific proteins, GGN1(gametogenetin protein 1), GGNBP1 (gametogenetin binding protein 1), GGNBP2 and OAZ3 (ornithine decarboxylase antizyme 3) form a novel testis-specific complex functioning in spermatogenesis. FANCL is involved in proliferation of PGCs in early embryo stage, and development of germ cells in adult.

Key words FANCL； germ cell；Fanconi anemia

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通讯作者 卢柏松 lubaisong@yahoo.com