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综 述

范可尼贫血与泛素化

张莹莹，周晓巍，黄培堂

军事医学科学院生物工程研究所, 北京 100071

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摘要 Fanconi贫血是一种罕见的隐性遗传性疾病，临床常以先天性畸形、进行性骨髓衰竭和遗传性肿瘤倾向为主要表现而确诊。FA病人细胞对DNA交联剂如丝裂霉素C（MMC）高度敏感。目前已经发现至少12种FA基因的缺失或突变能够引起FA表型的出现，其中10种相应的编码蛋白形成FA复合物共同参与FA/BRCA2 DNA损伤修复途径 — FA途径。FA核心复合物蛋白FANCL具有泛素连接酶活性，在结合酶UBE2T共同作用下，催化下游蛋白FANCD2单泛化，泛素化FANCD2与BRCA2形成新的复合物，修复DNA损伤。去泛素化酶USP1在DNA修复完毕后移除FANCD2的单体泛素，使因损伤修复而阻滞的细胞周期继续进行。机体很可能在不同信号通路对FANCD2泛素化/去泛素化的精细调节下，调控FA途径参与不同的DNA修复过程。

关键词 Fanconi贫血；FA 途径；泛素化；DNA损伤修复

分类号

Fanconi Anemia and Ubiquitination

Yingying Zhang, Xiaowei Zhou, Peitang Huang①

Beijing Institute of Biotechnology, *Beijing* 100071, *China*

Abstract

Fanconi anemia (FA) is a rare recessive hereditary disease characterized clinically by congenital defects, progressive bone-marrow failure, and cancer predisposition. Cells from FA patients exhibit hypersensitivity to DNA cross-linking agents, such as mitomycin C (MMC). To date, at least 12 FA genes have been found deleted or mutated in FA cells, and 10 FA gene products form a core complex involved in FA/BRCA2 DNA repair pathway-FA pathway. The ubiquitin E3 ligase FANCL, an important factor of FA core complex, co-functions with a new ubiquitin conjugating enzyme UBE2T to catalyze the monoubiquitination of FANCD2. FANCD2-Ub binds BRCA2 to form a new complex located in chromatin foci and then take part in DNA repair process. The deubiquitylating enzyme USP1 removes the mono-ubiquitin from FANCD2-Ub following completion of the repair process, then restores the blocked cell cycle to normal order by shutting off the FA pathway. In a word, the FANCD2 activity adjusted exquisitely by ubiquitination and/or deubiquitination in vivo may co-regulate the FA pathway involving in variant DNA repair pathway.

Key words Fanconi anemia FA pathway ubiquitination DNA repair

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通讯作者 amms832@126.com