Modeling Non-homologous End Joining

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Non-homologous end joining (NHEJ) is the dominant DNA double strand break (DSB) repair pathway and involves several NHEJ proteins such as Ku, DNA-PKcs, XRCC4, Ligase IV and so on. Once DSBs are generated, Ku is first recruited to the DNA end, followed by other NHEJ proteins for DNA end processing and ligation. Because of the direct ligation of break ends without the need for a homologous template, NHEJ turns out to be an error-prone but efficient repair pathway. Some mechanisms have been proposed of how the efficiency of NHEJ repair is affected. The type of DNA damage is an important factor of NHEJ repair. For instance, the length of DNA fragment may determine the recruitment efficiency of NHEJ protein such as Ku [1], or the complexity of the DNA breaks [2] is accounted for the choice of NHEJ proteins and subpathway of NHEJ repair. On the other hand, the chromatin structure also plays a role of the accessibility of NHEJ protein to the DNA damage site. In this talk, some mathematical models of NHEJ, that consist of series of biochemical reactions complying with the laws of chemical reaction (e.g. mass action, etc.), will be introduced. By mathematical and numerical analysis and parameter estimation, the models are able to capture the qualitative biological features and show good agreement with experimental data. As conclusions, from the viewpoint of modeling, how the NHEJ proteins are recruited will be first discussed for connection between the classical sequential model [4] and recently proposed two-phase model [5]. Then how the NHEJ repair pathway is affected, by the length of DNA fragment [6], the complexity of DNA damage [7] and the chromatin structure [8], will be addressed.

Reference


