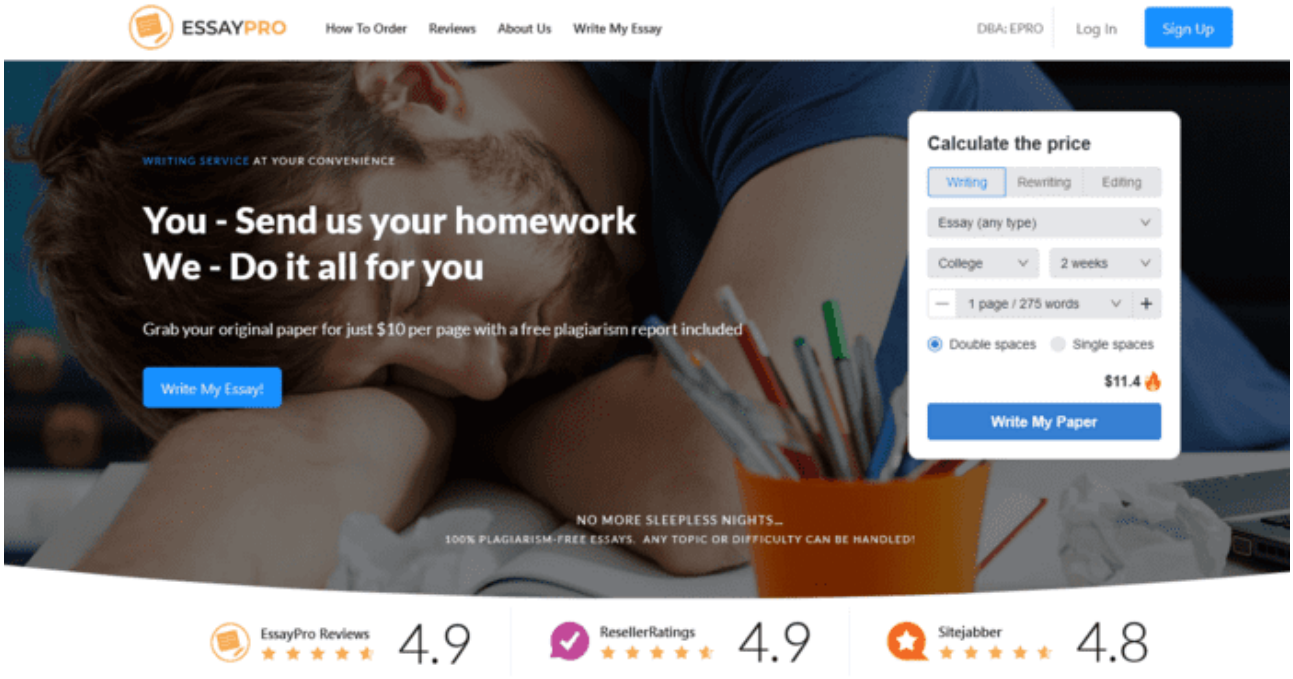
Fanconi Anemia Essay



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Fanconi Anemia (FA) is a hereditary recessive disorder that is characterized by defective DNA cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and cytogenetic instability. FA is caused by mutations in a complex set of proteins, including a FA core complex which contains eight out of sixteen known FA genes and their associated proteins. The FA proteins work together in a genome maintenance pathway called the FA/BRCA pathway, which plays an important role during the S phase of the cell cycle. The list FA complementation group (FANC) are: FANC-A, -B, -C, -D1/BRCA2, -D2, -E, -F, -G, -L, -I, -J/BRIP1,-M, -N/PALB2, -P/SLX4, -O/RAD51C and XPF. While the members of the FA complementation group do not share sequence similarity, they are related by their assembly into a common nuclear protein complex. Beside these sixteen FA proteins, there are several other proteins associating with the FA core complex, known as the FA Associated Proteins (FAAPs): -100, -24, -20, -16/MHF1, and -10/MHF2. FA plays an important role in the genomic stability through DNA repair of interstrand crosslinks (ICLs). When mutations occur in these genes, however, abnormal cell division, which eventually causes cancer and congenital defects occurs in most patients (Nalepa, et al., 2013; Tomida, et al., 2013).
Fanconi anemia is caused by mutations in one of the Fanconi anemia genes leading to lack of interstrand crosslink repair. In the process of DNA repairing, the interstrand

crosslinks is recognized by the complex of two proteins, FAAP24 and FANCM. These proteins participate in substrate binding and enable recruitment of the FA core complex. This core has E3 ligase activity and can monoubiquitinate (addition of o...

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...d DNA damage response pathway. EMBO J. 26: 2104–2114.
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