Abstract

Cells in the human body are constantly under stresses that cause DNA damage. Accumulation of unrepaired DNA damage can lead to mutations which, if in genes controlling cell cycle, apoptosis, or chromatin organization, can lead to cancer. Oxidative DNA damages are repaired by enzymes in the base excision repair (BER) pathway. hOGG1 is a DNA glycosylase in BER involved in the recognition and removal of the oxidative damage 8-oxoG opposite cytosine. Mutations affecting the glycosylase activity of hOGG1 have been shown to affect its ability to remove 8-oxoG opposite C, but have not previously been tested for effects in a cellular system. Here we report the effects on cells expressing the hOGG1 wild type or tumor associated germline variants R154H and R197W in the development of a transformed phenotype. Cells expressing R154H or R197W show increased colony formation in soft agar and have an increased proliferation rate as compared to wild type expressing cells. Additionally, hOGG1 variant expressing cells may show a mutator phenotype. Our findings suggest that heterozygous expression of these variants may lead to an increased cancer incidence.