

Gestational Mutations and Carcinogenesis

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Background and Aims: We present a mathematical formulation to evaluate the effects of gestational mutations on cancer risk.

Methods: The hazard or incidence function of cancer is expressed in terms of the Probability Generating Function (PGF) of the number of normal and mutated cells at birth. Using Filtered Poisson Process Theory, we obtain the PGF for several mechanistic models for the accumulation of gestational mutations. In particular, we develop expressions for the hazard function when one or two successive mutations could occur during gestation. We also calculate the hazard when the background gestational mutation rates are increased due to exposure to mutagens, such as prenatal radiation.

Results: To illustrate the use of our models, we apply them to colorectal cancer in the SEER database. We find that the proportion of cancer risk attributable to developmental mutations depends on age and that it could be quite significant when gestational mutation rates are high. The analysis of the SEER data also shows that gestational mutations could contribute to inter-individual variations in colorectal cancer risk.

Conclusions: Gestational mutations could have substantial impact on cancer risk if mutation rates are significant. Spontaneous mutations during gestation may be responsible for some of the heterogeneity of cancer risk in human populations. Our methodology can be used to estimate the effects of mutagen exposure during gestation on cancer risk. For adult onset cancers the largest risk of gestational exposure to mutagens appears to be conferred by exposure late during pregnancy.

References:

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