CYCLE STRUCTURE ANALYSIS PROVIDES EVIDENCE THAT SECONDARY ELECTRONS FROM HZE PARTICLES ADD BREAKS TO COMPLEX EXCHANGES FORMING ALONG PRIMARY PARTICLE TRACKS

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We have recently reported on experiments designed to measure chromosome aberrations in human cells following irradiation with γ-rays, α-particles and HZE ions. We found a linear dose response for alpha-particles in fibroblasts, which is typical for high LET radiations. In contrast, lymphocytes irradiated 1 GeV/amu ^{56}Fe ions produced a linear dose response for the aberrations themselves, but a curvilinear one for the chromosomal breakpoints that comprise these aberrations. This curvature was found to be linked to breakpoints associated with complex exchanges; those exchanges forming from three or more chromosome breaks. Careful analysis of the composition of larger complex exchanges (those originating from four or more breaks) suggested to us that these exchanges can be formed from breaks grouped into specific subsets that can interact independently from other breaks within the exchange. These subsets termed "rejoining cycles" contain specific numbers of breaks which determine their "cycle order" and designation (e.g. c2 for two breaks; c3 for three breaks etc.). There is a unique class of complex exchanges where all the breaks can only be grouped into a single rejoining cycle. But beyond that, it is impossible to determine with certainty the cycle structure on the basis combinatorial chromosome painting data alone (mFISH). With that said, we can, however, determine "obligate cycle structures" (OCS), which define cycles of the smallest number of breaks *obliged* to freely interact in time and space. In other words, such analysis produces the most conservative assignment of cycles, in terms of their size, necessary to characterize the exchange.

We performed OCS analysis on complex exchanges generated in our experiments and constructed separate dose responses for rejoining cycles of differing sizes. These results were fitted to the simple power functions ($Y = kD^n$), whereby dose responses having n>1 were considered to demonstrate curvature. Small obligate cycles (c2, c3 and c4) had linear dose responses following Fe ion irradiation, while larger structures (c5-c6) exhibited significant curvature. All α-particle dose responses were linear. These results imply that while a single ^{56}Fe primary track can produce cycles as large as c4, cycles of greater size will, more than likely, require the interaction of damage produced by multiple tracks. Since a dose of about 0.8 Gy produces, on average, one primary particle traversal per cell nucleus, it is unlikely that track interaction between two *primary particle tracks* will occur for the doses used in these experiments. However, we conclude that HZE ions—by virtue of their long-ranging *secondary electrons* (delta rays)—are capable of interacting with distant separate primary particle tracks. This leads to curvature that results from the addition of breaks to exchanges as they form along these tracks. This work was supported by a grant from NASA (NNJ04HD83G).