Chromatin dynamics in DNA repair

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A single double-strand break (DSB) can kill a cell. Consequently, cells have evolved a plethora of repair and signalling proteins that converge to DSBs to trigger repair and cell cycle arrest. In budding yeast, most DSBs are repaired through homologous recombination, a process by which the broken DNA uses genetic information contained in a homologous sequence which can be located anywhere in the genome. How a broken piece of DNA looks for and finds its homologous template for repair is unknown. Here, we are testing the hypothesis that chromatin movement promotes the search for homology during double strand break repair. We first modeled how movement and nuclear location could affect homology search. We find that movement and attachment to the nuclear periphery would increase the efficiency of homology search. Then, we defined the biophysical properties of the movement of repair foci by quantitative fluorescence microscopy and found that spontaneously occurring repair foci marked with Rad52-YFP have a low diffusion coefficient and move within a volume that is only about 5% that of the nucleus. Conversely, a DSB induced by an endonuclease has a diffusion coefficient that is nearly 2 fold higher and can roam around 2/3 of the nuclear volume. In addition to identifying repair proteins involved in keeping the movement of spontaneous foci low, we show that the movement does not appear to be merely the consequence of the repair process. Finally, we found that different types of damage to DNA lead to repair foci with different diffusion properties. We speculate that cells might have the capacity to regulate the movement of repair foci.