Lack of G1/S control in *swi6Δ* mutants destabilizes the genome of *S. cerevisiae* via replication stress-induced DSBs and Rad51-mediated illegitimate recombination

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The protein *Swi6* in *Saccharomyces cerevisiae* is a cofactor in two complexes that regulate the transcription of the G1/S transition genes. It also ensures proper oxidative and cell wall stress responses. Our previous study identified *SWI6* among genes linked to oversensitivity to radiomimetic zeocin, i.e., genes important for surviving double-strand break (DSB) stress. The *swi6*Δ/*swi6*Δ strain belongs to a very limited group of knock-out strains with high sensitivity to DSBs induced both chemically and by the *in vivo* overexpression of homing endonucleases. This group also comprises strains lacking XRS2 or RAD52, whose products are crucial in DSB repair. Moreover, one of our previous whole-genome screens also identified the *swi6*Δ/*swi6*Δ strain as a spontaneous mutator, indicating an important role of *Swi6* in maintaining genome stability not only under genotoxic stress but also during unperturbed cell growth. Results we have got recently showed that *swi6*Δ mutants are genetically unstable and the source of this instability is the replication block that leads to double-strand break (DSB) formation. The cellular pathway that enables the repair of replication-born DSBs is the Rad51-dependent illegitimate recombination. Using this repair pathway increases the chance to survive DNA damage because it allows replication to resume. However, it also leads to genome rearrangements, which subsequently generate the division problems, which again leads to poor growth and increased mortality. We also noticed the differences between *swi6*Δ haploid and *swi6*Δ/swi6Δ diploid yeast cells in the molecular outcomes of replication block, which are not limited to different scenarios of replication block resolution but include different adverse effects of the absence of the *Swi6* protein in haploid vs. diploid cells on mutation frequency in the forward mutation assay. The overexpression of *SWI4* or PAB1 partially suppresses the *swi6*Δ cells oversensitivity to genotoxic agents. However, only overexpression of one of them can overcome another *swi6*Δ mutation phenotypic hallmark; the DNA content aberrations can be cured only by the overproduction of *SWI4* and not by PAB1.

Speaker Biography

Skoneczna A has completed her PhD from Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Poland. She is the Professor of Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland. She leads her group in the Laboratory of Mutagenesis and DNA Repair. She has over 30 publications that have been cited over 460 times, and her publication H-index is 12 and has been serving as a reviewer of reputed journals, as well as in National Science Centre and The National Centre for Research and Development.

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