in different locations, in succession of each other, is limited to a just few SSBs spots. The cell appears to recruit very large number of copies of XRCC1 and PCNA to the first detected lesion rather than spread the resources over all the lesions. In early and late S-phase, when the number of damage sites exceeds approximately 3, the available PCNA pool appears to be exhausted, while recruitment of XRCC1 is still detectable. This suggests switching repair mechanisms from long to short patch.

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T-1. Analysis of nuclear actin in human progeria cells.

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Hutchinson-Gilford progeria syndrome (HGPS) is a rare premature disorder caused by de novo single base substitution in the lamin A gene. Lamin A contributes to nuclear architecture and spatial organization of chromatin in the nucleus. The lamin A mutant in HGPS cells is called progerin. The expression of progerin leads to functional and structural disruption of nuclear organization. In HGPS cells, several nuclear defects are observed such as irregular nuclear shape and increased DNA damage. By *in vitro* assay, it was shown that lamin A directly interacts with actin in the nucleus [1]. Actin is abundantly present in cytoplasm and is involved in multiple cellular functions. In addition, some actin exists in the nucleus as monomeric globular (G-) actin and polymerized filamentous (F-) actin. Nuclear actin has roles in epigenetic regulation. For instance, nuclear F-actin is involved in transcriptional regulation, DNA damage repair, and activation of Wnt/beta-catenin signaling [2]. Since progerin lacks actin binding sites [1], we hypothesized that the expression of progerin impairs functions and dynamics of nuclear actin, and that these nuclear actin dysfunctions are relevant to HGPS phenotypes. Thus we analyzed nuclear actin in HGPS cells. In this research, we analyzed human dermal fibroblast cells, which inducibly express GFP-progerin by doxycycline (Dox) as HGPS model cells [3]. When we observed nuclear F-actin, we found that the HGPS cells contains less nuclear F-actin as compared to control cells, in which progerin expression is not induced. Consistent with this observation, the activity of a Wnt/beta-catenin targeting promoter is reduced in the HGPS cells. Next, to test the possibility that the reduction of nuclear F-actin is relevant to HGPS phenotypes, we artificially increased nuclear F-actin by expressing NLS (nuclear localization signal)-tagged actin in the HGPS cells. It was observed that the irregular nuclear shapes of the HGPS cells were complemented by the expression of NLS-actin. These results suggest that reduction of nuclear

F-actin caused by the expression of progerin is, at least partly, relevant to HGPS.

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T-2. Activation of NF-kappaB differentially affects the proliferation rate of different non-small cell lung carcinoma cell lines

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Activity of NF-kappaB transcription factor is usually associated with stimulation of the proliferation potential of cancer cells. On the contrary, our preliminary data suggest that sustained activation of NF-kapp has an opposite effect on certain cell lines. Our research is aimed to dissect mechanisms behind the pro- and anti-proliferative effects of NF-kappaB in non-small cell lung carcinoma (NSCLC) cell lines. Methods: To avoid pleiotropic effects of extracellular stimuli, like TNF or EGF growth factors, we established NSCLC cell lines H1299 and H23 with constant overexpression of the RELA gene, which encodes the primary activation subunit of NF-kappaB. Expression analysis of target genes with qRT-PCR confirmed that H1299/RelA and H23/RelA cell lines maintained enhanced transcriptional activity of the exogenous RelA/p65. The rate of Proliferation, colony formation capacity, cell cycle, apoptosis rate, cellular senescence and expression of genes controlling the cell cycle were investigated. Results: We found that RELA overexpression suppressed proliferation of the H1299 cell culture. The RELA expression level and NF-kappaB transcriptional activity demonstrated inverse correlation with the proliferation rate. Similar results were obtained with the colony formation assay. The cells with high RELA expression had reduced ability to form individual colonies. We than tested a direct involvement of RelA/p65 in the cell cycle control or induction of apoptosis but neither cell cycle nor apoptosis rate were affected. Similarly, the expression analysis of genes involved in regulation of cell cycle and apoptosis (p21/WAF1, PUMA, BAX) did not reveal any difference. However, the SA-b-gal staining indicated that H1299/RelA had higher rate of cellular senescence comparing to the parental cell line. To test whether the negative impact of NF-kappaB activation is common for other NSCLC cell lines, we analyzed effects of RELA overexpression in another NSCLC cells, H23. In contrast to H1299 cells, sustained NF-kappaB activation in H23 cells led to an enhanced proliferation rate. Further investigations of possible mechanisms behind the differences in NF-kappaB activation between the H1299 and H23 cell lines are in the progress. Conclusions: We demonstrated that constant NF-kappaB activation might either suppress or stimulate proliferation of different NSCLC cells. The effect does not involve cell cycle control or apoptosis but may implicate cellular senescence. Considering that H1299 and H23 cells lines differ in p53 status, further investigation of NF-kappaB may reveal novel aspects of NF-kappaB/interplay in NSCLC.