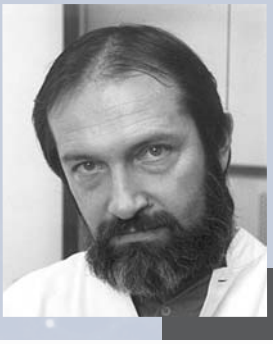

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Laboratory of Genome Integrity

DNA damage response, cell cycle, oncogenic transformation

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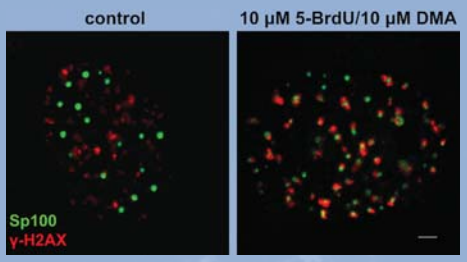
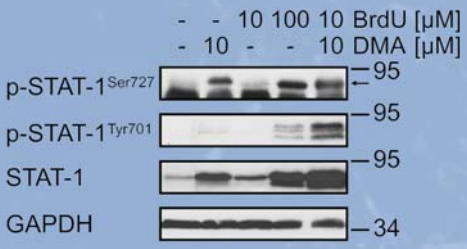


Foci of DNA damage (γ-H2AX) colocalize with PML nuclear bodies (Sp100) in prematurely senescent cells



Activated markers of JAK/STAT signalling pathway in HeLa cells forced to premature senescence by 5-bromodeoxyuridine and/or distamycin A

Research topics

The newly established group will be centered on the mechanisms of maintenance of genomic integrity, which is a fundamental biological mechanism that guards against genetic diseases including cancer. Orchestration of DNA damage signalling with cell cycle checkpoints, DNA repair, chromatin modulation and cell death pathways relies on regulatory protein post-translational modifications. The key role of protein phosphorylation in DNA damage response (DDR) is well established, however, the significance of ubiquitylation, sumoylation and neddylation is only emerging. We will focus on human genes involved in regulatory ubiquitylation, sumoylation and neddylation within the DDR machinery. We will study the molecular basis and biological role of such protein modifications in DNA damage signalling and cell fate decisions including cell cycle arrest, DNA repair and cell survival.

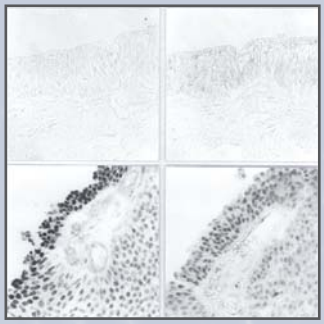
The second aim of our work will be focused on the mechanisms of cellular senescence, the regulatory pathways involved in specific secretion phenotype of senescent cells and pathophysiological role of senescent cells in tumour and ageing tissues. We will be addressing specific functions of PML and PML nuclear bodies in development of senescent phenotype, the role of interferons in transcription regulation of *PML* gene and other interferon-stimulated genes in senescent cells.

Current grant support

GA AS CR (IAA50039050), GA CR (204/08/1418, 301/08/0353).

Selected recent papers

So far no papers (a newly formed group)



Immunohistochemical section of normal bladder mucosa (top row) and early bladder cancerous lesion (Ta stadium; bottom row) stained by activated form of Chk2 kinase (left) and heterochromatin marker HP1γ (right).

Nucleoli-associated PML nuclear bodies are characteristic for replicatively senescent untransformed cells and can be induced in prematurely senescent tumour cell lines by 5-bromodeoxyuridine and distamycin A.