



# Laboratory of Recombination and DNA Repair

/ Department of Biology / National Centre for Biomolecular Research  
/ Faculty of Medicine and Faculty of Science / Masaryk University



RESEARCH GROUP CONTACT >>

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## THEMATIC RESEARCH FOCUS >

### RESEARCH AREA

- » DNA repair processes
- » Mitotic and meiotic recombination
- » Posttranslational modification of proteins
- » Induced pluripotent cells
- » Genomic instability

### EXCELLENCE

- » Biochemical and molecular characterization of proteins involved in DNA Repair, Recombination and Replication

### MISSION

- » Biochemistry of recombinant proteins and molecular dissection of their action
- » Molecular characterization of processes responsible for DNA repair and genomic instability
- » Targeting critical steps in these processes for therapeutical purposes
- » Education and training of young scientists

## DEVELOPED TECHNOLOGIES >

### CONTENT OF RESEARCH

- » Regulation of homologous recombination
- » Role of structure-specific nucleases in DNA repair
- » Role of mediator proteins during recombination and repair
- » Initiation of DSB formation and its processing
- » Multi-functional role of Srs2 in recombination and DNA repair

- » DNA repair synthesis
- » Role of helicases in genomic instability
- » Induced pluripotent cells

### MAIN CAPABILITIES

- » Biochemical and molecular characterization of biological processes
- » Identification of specific genes as targets for therapeutical use
- » Screening and identification of inhibitors of targeted enzymes involved in genome instability and their further optimization and characterization with an aim to specifically affect tumour cells

### FIELDS OF RESEARCH RESULTS APPLICATION

- » Molecular biology - understanding molecular mechanisms of processes related to genomic stability
- » Biochemistry – characterization of proteins involved in DNA repair
- » Medicine – potential substances for treatment of cancer and other genome instability based diseases

### ALUMNI PROFILE

The graduate has knowledge about DNA repair processes, genome stability and biochemistry of proteins involved in DNA repair.

#### Knowledge and skills:

1. Biochemistry (protein expression and purification, basic biochemical characterization, protein-protein interactions, protein-DNA interactions, enzymology)
2. Molecular biology (cloning, mutagenesis, two-hybrid system, CHIP, Co-IP)
3. Stem cell research (cell cultures, iPS, cell differentiation)



## NUMBER OF RESEARCH POSITIONS ↘

### SENIOR RESEARCH STAFF

6

### JUNIOR RESEARCH POSITIONS (INCL. PH.D. STUDENTS)

10

## KEY RESEARCH EQUIPMENT ↘

### LIST OF DEVICES

#### Instrumentation for spectral analysis:

- » Microtitration plate readers
- » Spectrophotometers
- » Spectrofluorometer
- » Spectropolarimeter

#### Instrumentation for interactions studies:

- » Isothermal titration calorimeter
- » SPR machine

#### Chromatography facilities:

- » 4 FPLC
- » Static light scattering system

#### Microscopy:

- » Conventional fluorescence
- » Laser confocal microscope

#### Single molecule analysis:

- » Optical tweezers
- » AFM
- » Microscope with TIRF objective

#### Additional equipment:

- » 2-D electrophoresis set
- » Thermocyclers
- » Geldoc system
- » Chemiluminiscent documentation system
- » Themoblocks
- » Large scale incubators
- » Centrifuges
- » Ultracentrifuge autoclaves
- » Deep freezers

We are planning to buy a piece of equipment for the single-molecular observation of proteins and DNA.

## BUDGET ↘

### TOTAL (MIL. CZK/ MIL. EUR)

7 / 0,28

### PART OF THE TOTAL BUDGET FROM PRIVATE RESOURCES (%)

0

### PART OF THE TOTAL BUDGET FROM FOREIGN RESOURCES (%)

60

## MAIN PROJECTS ↘

- » **2010–2012:** The role of post-translational modification in DNA repair and recombination: Meiosis, SUMOylation and Zip3 protein (project ME10048 financed by the Ministry of Education, Youth and Sports)
- » **2009–2011:** Resolution of replication-recombination DNA intermediates and its role in genomic instability (project GA301/09/1917 financed by the Czech Science Foundation)

## ACHIEVEMENTS ↘

- » Wellcome International Science Fellowship (2005)
- » EMBO/HHMI Fellowship (2005)

#### Publications:

- » Krejci, L.\*, Van Komen, S., Li, Y., Villemain, J., Reddy, M. S., Klein, H., Ellenberger, T., Sung, P. (2003) DNA helicase Srs2 disrupts the Rad51 presynaptic filament. *Nature* 423:305-9.
- » Papouli, E., Chen, S., Davies, A.A., Huttner, D., Krejci, L., Sung, P., Ulrich, H.D. (2005) Crosstalk between SUMO and Ubiquitin on PCNA is mediated by recruitment of the Helicase Srs2p. *Mol. Cell* 19(1): 123-33.
- » Antony E, Tomko EJ, Xiao Q, Krejci L, Lohman TM, Ellenberger T. (2009) Srs2 disassembles Rad51 filaments by a protein-protein interaction triggering ATP turnover and dissociation of Rad51 from DNA. *Mol Cell*. 10;35(1):105-15.
- » V. Altmannova, N. Eckert-Boulet, M. Arneric, P. Kolesar, R. Chaloupkova, J. Damborsky, P. Sung, X. Zhao, M. Lisby and L. Krejci \* (2010) Rad52 SUMOylation affects the efficiency of the DNA repair. *Nucleic Acids Res.* 38 (14): 4708-21.

## MAIN COLLABORATING PARTNERS ↘

### COLLABORATION WITH ACADEMIC PARTNERS

- » Cancer Research Centre (London, GB)
- » Columbia University (New York, US)
- » F.I.R.C. Institute of Molecular Oncology (Milan, IT)
- » Hungarian Academy of Sciences (Budapest, HU)
- » IFOM (Milan, IT)
- » IMP-IMBA Research Center (Vienna, AT)
- » Institute of Molecular Genetics, AS CR (Prague, CZ)



- » Institute of Scientific Instruments, AS CR (Brno, CZ)
- » Memorial Sloan-Kettering Cancer Center (New York, US)
- » New York University (New York, US)
- » Technical University of Denmark (Copenhagen, DK)
- » University of California (Davis, US)
- » University of Copenhagen (Copenhagen, DK)
- » University of Oxford (Oxford, GB)
- » Washington University (St. Louis, US)
- » Yale University (New Haven, US)

## EXPECTATIONS ↘

### REQUIREMENTS

- » Structural characterization of proteins
- » Single-molecule analysis (AFM, Optical or Magnetic tweezers)
- » Microscopy methods (EM, SLIM, FRET)
- » Microfluidics

### OFFERS

- » Biochemistry of proteins
- » Small/medium/large scale protein production
- » In vitro assays for nuclease/helicase/polymerase inhibitors

