DEPARTMENT OF MOLECULAR EMBRYOLOGY

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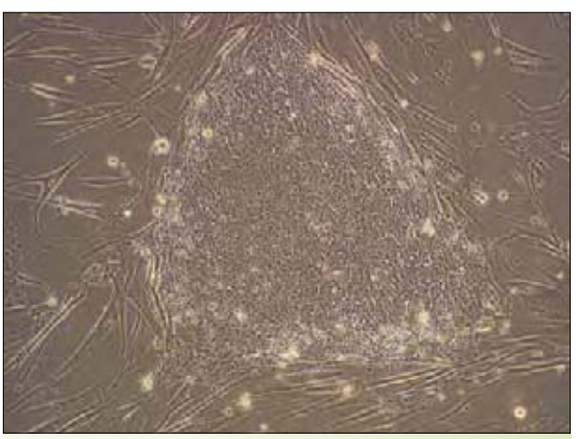
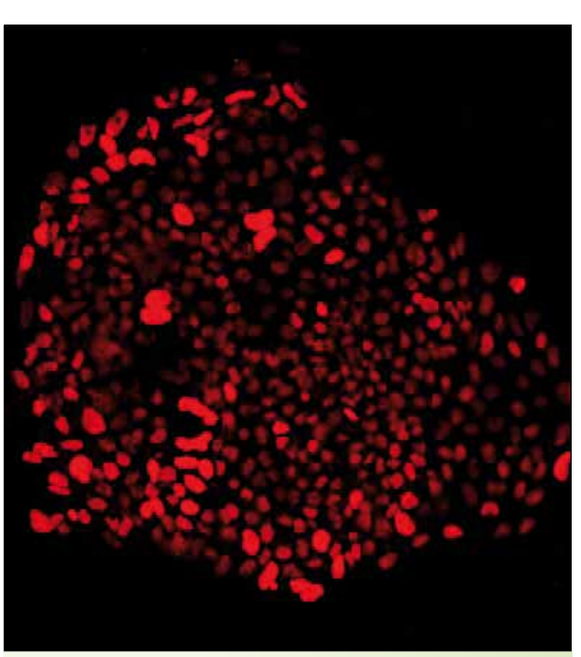
RESEARCH TOPICS

Historically, research in the department has focused on studying cells with pluripotent properties, including developing gametes and cells of embryonal origin – embryonal carcinoma cells and embryonic stem cells. The department is the first and only laboratory in the Czech Republic where cell lines (embryonic stem cells – ESC) were established from human blastocyst-stage embryos in 2003.



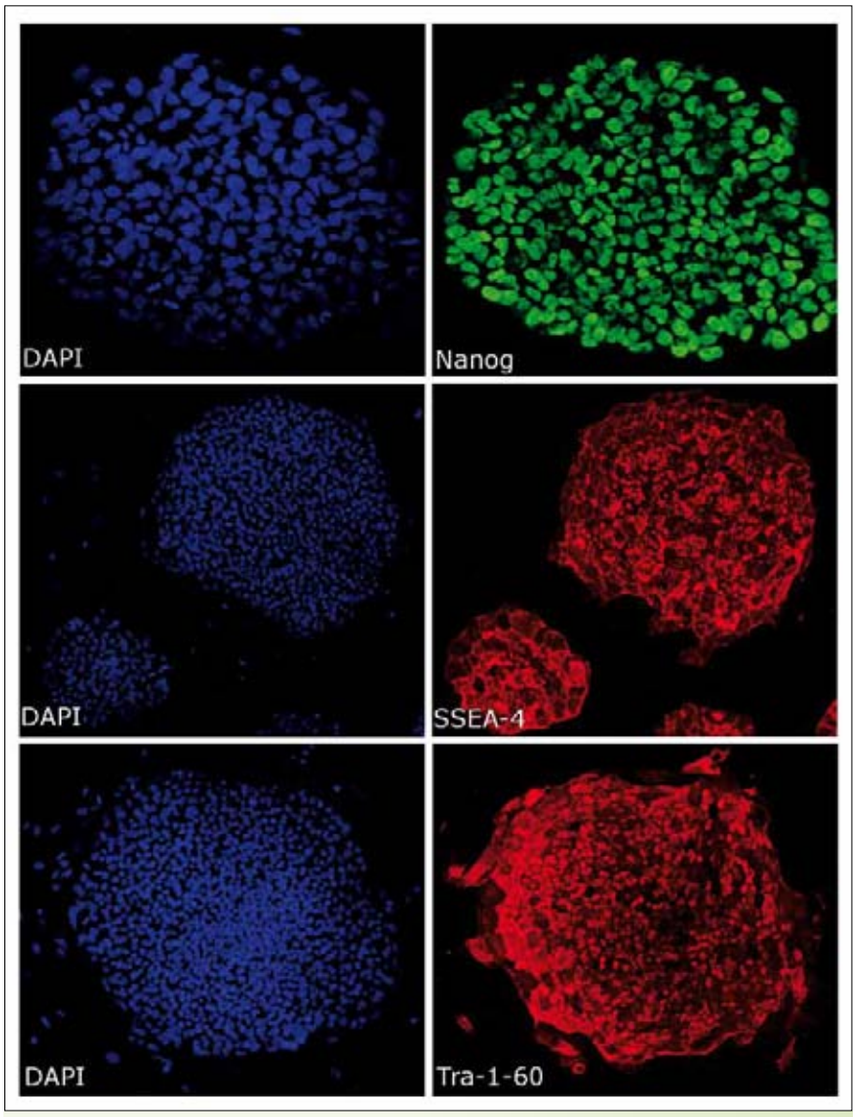
Colony of undifferentiated human embryonic stem cells *(line CCTL14 established in the department) growing on a feeder layer of mouse embryonic fibroblasts.*

Since then, the major focus of the department has been on various aspects of the biology of these unique primitive cells, which, because of their potential to differentiate into all specialized cell types of the adult body, represent unprecedented promise for new-age medicine.

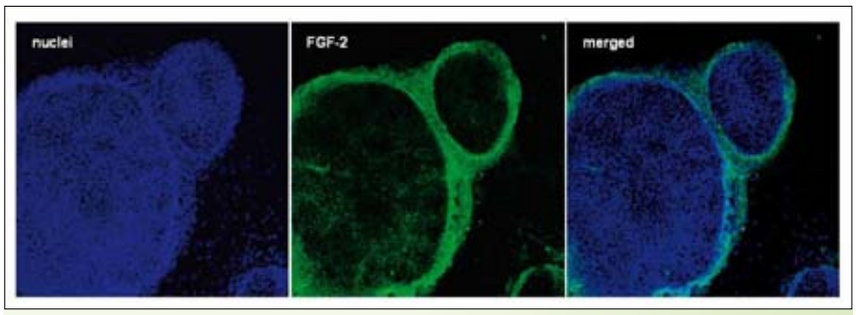


Tumor suppressor *protein p53 is highly expressed in the nuclei of some cells in a colony of human embryonic stem cells cultured in vitro. The red color visualizes p53 protein inside the cell nuclei.*

Most importantly, we investigate i) the functioning of cell cycle regulatory molecules, CDKs, cyclins, and CKIs, and their significance for the undifferentiated growth of human ESC (hESC), ii) the molecular pathways that are employed by hESC to transmit signals produced by fibroblast growth factor (FGF-2) and their biological role in this cell type, and iii) the molecular mechanisms that underlie the genetic alterations occurring in hESC propagated in culture and the phenotypical changes produced by such damage to the hESC genome. Besides the research focused on the molecular and biological properties of hESC, we also conduct experiments that target more clinically relevant issues, which include mainly the development of new protocols and conditions for the propagation of undifferentiated hESC and/or their differentiation into specific functional cell types. We have established fruitful collaborations with several renowned laboratories around the world and participate in various international studies aimed at exploiting the potential of hESC. Among them, a global comparative study lead by Prof. Peter Andrews (University of Sheffield) called the International Stem Cell Initiative is the most significant.



The presence of pluripotency markers *(transcription factor Nanog; cell membrane glycoproteins SSEA-4, TRA-1-60) in undifferentiated human embryonic stem cells as visualized by indirect immunofluorescence followed by confocal microscopy. Blue – cell nuclei, green/red – markers.*



Expression of fibroblast growth factor (FGF-2) in human embryonic stem cells. *The expression is higher in differentiating cells at the periphery of the cell colonies. Blue – cell nuclei, green – FGF-2.*

CURRENT GRANT SUPPORT

EU 6th FP, 018739, Platforms for biomedical discovery with human ES cells, ESTOOLS.

Ministry of Education, 1M0538, Center of Cell Therapy and Tissue Repair.

GA CR, 204/09/2044, and MRC International Stem Cell Initiative II.

SELECTED RECENT PUBLICATIONS

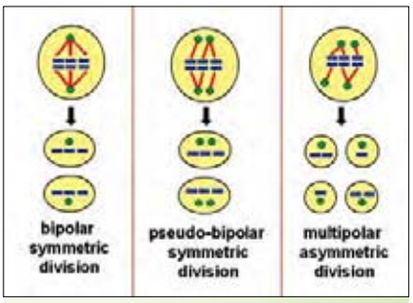
1. Bryja V, Čajánek L, Pacherník J, Hall AC, Horváth V, Dvořák P, Hampl A. (2005) Abnormal development of mouse embryoid bodies lacking p27Kip1 cell cycle regulator. Stem Cells 23: 965–974.

2. Dvořák P, Dvořáková D, Košková T, Vodinská M, Najvirtová M, Krekáč D, Hampl A. (2005) Expression and potential role of fibroblast growth factor 2 and its receptors in human embryonic stem cells. Stem Cells 23: 1200–1211.

3. Dvořák P, Dvořáková D, Hampl A. (2006) Fibroblast growth factor signaling in embryonic and cancer stem cells. FEBS Lett 580: 2869–2874.

4. Evsikov AV, Graber JH, Brockman JM, Hampl A, Holbrook AE, Singh P, Eppig JJ, Solter D, Knowles BB. (2006) Cracking the egg: Molecular dynamics and evolutionary aspects of the transition from the fully grown oocyte to embryo. Genes & Dev 20: 2713–2727.

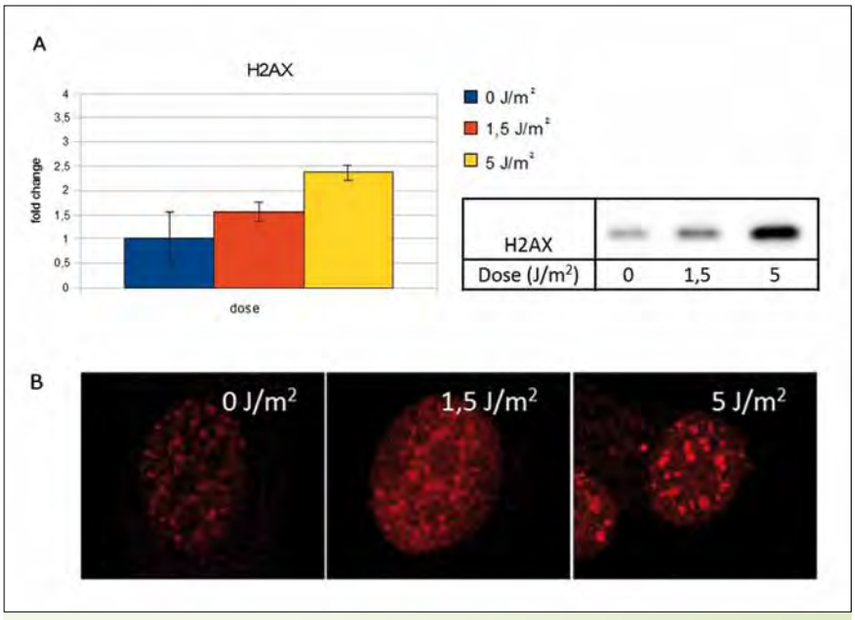
5. Adewumi O, Aflatoonian B, Ahrlund-Richter L, Amit M, Andrews PW, Beighton G, Bello PA, Benvenisty N, Berry LS, Bevan S, Blum B, Brooking J, Chen KG, Choo AB, Churchill GA, Corbel M, Damjanov I, Draper JS, Dvořák P, Emanuelsson K, Fleck RA, Ford A, Gertow K, Gertsenstein M, Gokhale PJ, Hamilton RS, Hampl A, Healy LE, Hovatta O,



Schematic of the potential outcomes of overamplification of centrosomes.

Hyllner J, Imreh MP, Itskovitz-Eldor J, Jackson J, Johnson JL, Jones M, Kee K, King BL, Knowles BB, Lako M, Lebrin F, Mallon BS, Manning D, Mayshar Y, McKay RD, Michalska AE, Mikkola M, Mileikovsky M, Minger SL, Moore HD, Mummery CL, Nagy A, Nakatsuji N, O'Brien CM, Oh SK, Olsson C, Otonkoski T, Park KY, Passier R, Patel H, Patel M, Pedersen R, Pera MF, Piekarczyk MS, Pera RA, Reubinoff BE, Robins AJ, Rossant J, Rugg-Gunn P, Schulz TC, Semb H, Sherrer ES, Siemen H, Stacey GN, Stojkovic M, Suemori H, Szatkiewicz J, Turetsky T, Tuuri T, van den Brink S, Vintersten K, Vuoristo S, Ward D, Weaver TA, Young LA, Zhang W. (2007) Characterization of human embryonic stem cell lines by the > International Stem Cell Initiative. Nat Biotechnol 25(7): 803–816.

6. Bryja V, Pacherník J, Vondráček J, Souček K, Čajánek L, Horvath V, Holubcová Z, Dvořák P, Hampl A. (2008) Lineage specific composition of cyclin D-CDK4/CDK6-p27 complexes reveals distinct functions of CDK4, CDK6 and individual D-type cyclins in differentiating cells of embryonal origin. Cell Prolif 41: 875–893.



Expression of H2AX protein in neural precursors *differentiated from human embryonic stem cells upon damage to their DNA caused by UVC irradiation. A – quantity of H2AX as determined by western blot. B – visualization of H2AX foci (red) inside the cell nuclei.*

Multipolar mitosis in a human embryonic stem cell *suffering from overamplified centrosomes as visualized by indirect immunofluorescence followed by confocal microscopy. Blue – chromosomes, red – microtubules of the mitotic spindle, green – centrosomes.*

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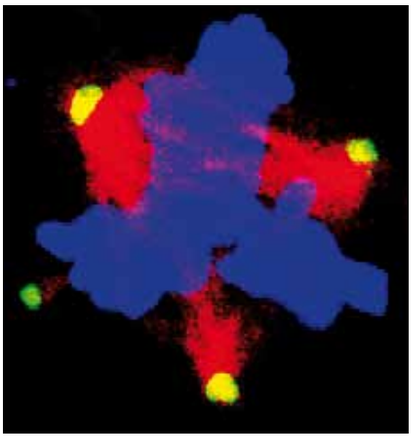

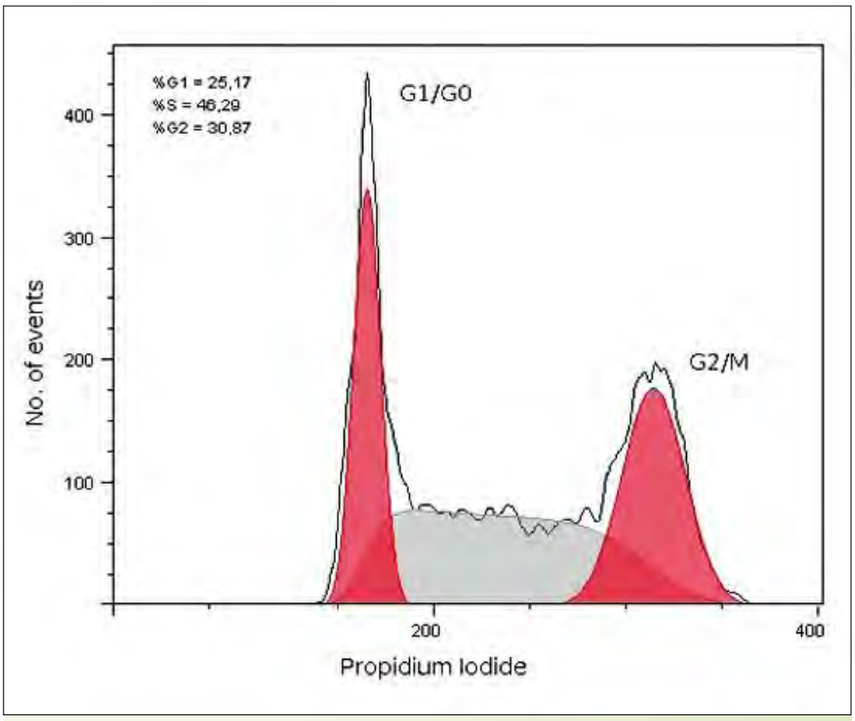

Distribution of undifferentiated human embryonic stem cells *in the phases of the cell cycle as determined by flow cytometry upon visualization of DNA content by propidium iodide staining (A)*

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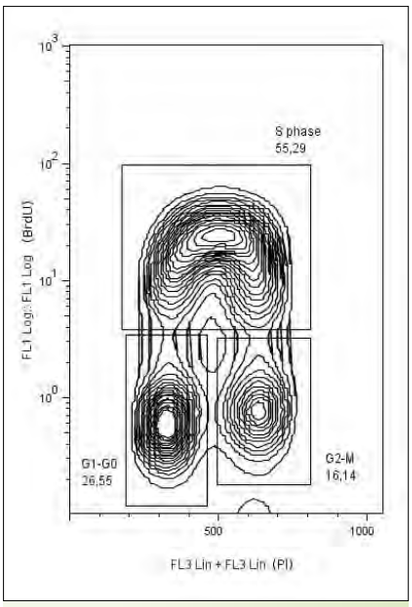

and upon metabolic labeling of DNA with BrdU combined with propidium iodide staining (B).