



# *Histology & Embryology Periodical*

*Department of Histology and Embryology*

*Third Faculty of Medicine, Charles University in Prague*

Volume 3, Issue 3

**December/January**

**2015/16**

## *In this issue:*

*Dear students...*

*Histology Slide Testing*

*Who is who? Part III*

Department of Histology & Embryology

*Image of the Month*

Sarcomere

*Theme:*

Revolution in biology:

CRISPR-Cas9

*Series:*

Endocrine Disruptors

Introduction

*Poem of the Month*

Moods by Jack London

*Eponyms*

Franz Nissl (1860-1916)

## ***Dear students...***

Into the examination period in between winter and summer semesters, comes another issue of your Periodical. The winter semester was an exciting time for both students, bending over their microscopes, and teachers hoping you are able to see there more than just pink and blue. We also hope you have transformed your excitement into knowledge and can demonstrate that knowledge throughout the coming tests and examinations.

Not just individual students, but also entire scientific areas, undertake exciting, transformative times. The most revolutionary today is happening in molecular biology. A new tool for gene editing discovered only a few years ago has taken a fascinating ride with unexpected speed. What is going on? Take a bite of **CRISPR-Cas9** and find out in this issue.

Communication on a cellular level is an essential function of all living organisms. Organisms communicate via sound, sight, smell or touch, but within organisms signaling happens mostly with chemical or electric stimuli. Most vertebrates have developed three systems that use chemical signaling; endocrine, nervous and immune. Compounds that interfere with the correct signaling and normal

function of hormones, particularly during development, are called **endocrine disruptors**. In this issue you can read an introduction to today's most active area of teratology.

You have read personal stories and messages from your tutors and lecturers in the previous issues; [here](#) and [here](#). In this issue "Who Is Who?" you can read a few encouraging words from two of your senior colleagues and instructors, Michal Schmalz and Jan Kolcava.



Figure 1 Václav Havel, Mick Jagger and Keith Richards in Prague in 1990.

Four year ago, in December 2011, Czech president and dissident **Václav Havel** died. To commemorate his legacy, throughout this issue you are going to find various excerpts from his plays and books, provided by the [Vaclav Havel Library](#).

Dear students, I hope you find the issue inspiring and thought provoking,

Klára Matoušková, editor

\*\*\*

## Histology Slide Test

Winter semester

Academic year 2015/16

### Organization:

Each student will receive three histological slides and one electron micrograph, and will be required to draw his/her own sketch of the tissue structures (just as in the Workbook, list 144.1 – 322.38). Time for reviewing the slides and preparation of the sketch will be fifteen minutes at the minimum.

Student will proceed to one of the examining faculty to identify correctly all three slides and the structures of the tissue (e.g. neurons in the cortex of brain, ducts of an exocrine gland). See your Workbooks for further guidance and details required. Students must demonstrate a clear understanding and good base knowledge of the tissue, too.

In the following part of the examination, students will identify the organelles on the electron micrograph and explain about their function in a cell or a tissue.

*„In short, Being has a memory. And thus even my insignificance – as a bourgeois child, a laboratory assistant, a soldier, a stagehand, a playwright, a dissident, a prisoner, a president, a pensioner, a public phenomenon, and a hermit, an alleged hero but secretly a bundle of nerves – will remain here for ever, or rather not here, but somewhere. But not, however, elsewhere. Somewhere here.*

Václav Havel:  
Diary entry for 5. December 2005,  
To the Castle and Back, 2006

Finally, students must satisfactorily explain the sketch of the tissue structure they have drawn during the earlier part of the examination.

\*

## Regular slots for Histology Slide Testing:

Tuesday **January 26**, 2016

9-12am and 1-3pm in approximately 20-minute intervals (e.g. 9.00-9.20am)

Wednesday **January 27**, 2016,

9-12am and 1-3pm

Thursday **January 28**, 2016

9-12h+13-15h

Friday **January 29**, 2016

9-12am and 1-3pm

Tuesday **February 2**, 2016

9-12am and 1-3pm

Wednesday **February 3**

9-12am and 1-3pm

Tuesday **February 9**, 2016

9-12am

Wednesday **February 10**

9-12am

Tuesday **February 16**

8-12am

Wednesday **February 17**, 2016

8-12am

\*

## Retake slots for Histology Slide Testing:

Tuesday **February 9**, 2016

3-7pm, approximately four students per hour

Wednesday **February 10**, 2016

3-7pm, approximately four students per hour

**Histology Slide Examination will take place in a practice room no 319.**

\*\*\*

## Who is who? Part III

Department of Histology & Embryology

Students - Instructors:

**MUC. Michal Schmalz**

General Medicine, 5<sup>th</sup> year student

*„To tell you the truth, it's not just Americans and other foreigners who think of me as a kind of fairy-tale prince or at least as the main character in a fairy tale; I too am often aware of something utterly unbelievable in my own destiny. And I'm less and less able to understand that destiny; at times I even see myself as a minor freak of history.“*

Václav Havel:  
Diary entry for 22. April 2005,  
To the Castle and Back, 2006

*Hi, my name is Michal. I have been an instructor at the Department of Histology and Embryology for three years already.*

*It is not like I have always liked histology. Only during the third semester have I gone from “I see nothing, seriously!” to „Look at the pink!“, all the way to „See, there are cells, and layers, and different staining and structures and ... Wow!“.*

*And this is exactly what I like about histology; it disguises many surprises and moments of astonishment. For the longest time you cannot believe your own eyes and all of a sudden, you see what were supposed to see in the first place!*



*Regarding recommendations for the following years of your med studies, I suggest you regularly visit the lectures from Propedeutics of Internal Medicine. Those presented by experienced medical doctors, during the fourth, fifth and sixth semester, are especially great as the lecturers are plenty knowledgeable and very few students actually come!*

*Michal Schmalz*

**MUC. Jan Kolčava**

General Medicine, 5th year student

*Hi, I'm a 10<sup>th</sup> semester med student and this is my third year as an instructor at the Department of Histology and Embryology of the 3<sup>rd</sup> Faculty of Medicine in Prague.*

*Honestly, I only became fond of histology after a failure during my first examination. Dr. Maňáková kicked me out saying „you should drink less and study more“.*

*Histology seems attractive to me with its order and significance. Besides histology I enjoy neuroscience, too.*

*I look forward to seeing you during our practicals and wish you are never afraid to ask. The same silly question you have we, as junior students, used to have, too. And a lecture is a better time to ask them then during an exam.*

*Jan Kolčava*

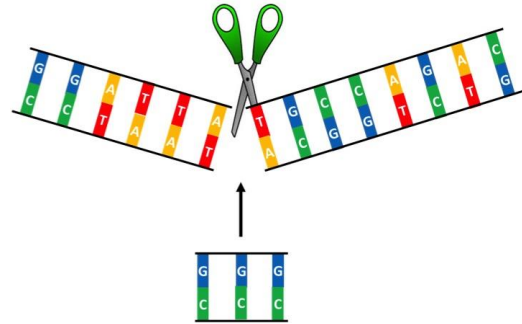
\*\*\*

*„Technology – that child of modern science, which in turn is a child of modern metaphysics – is out of humanity's control, has ceased to serve us, has enslaved us and compelled us to participate in the preparation of our own destruction. And humanity can find no way out: we have no idea and no faith, and even less do we have a political conception to help us bring things back under human control. We look on helplessly as that coldly functioning machine we have created inevitably engulfs us, tearing us away from our natural affiliations (for instance, from our habitat in the widest sense of that word, including our habitat in the biosphere) just as it removes us from the experience of Being and casts us into the world of “existences”.“*

Václav Havel:  
Power of the Powerless – samizdat essay, October 1978

Theme:

## Revolution in biology: CRISPR-Cas9



CRISPR-Cas9 is an instrument of DNA editing that has been extensively reported on in both scientific and pop media. The reason is that CRISPR-Cas9, unlike its' predecessors, enables genome editing that is comparatively simple, quick and affordable. And such qualities makes CRISPR-Cas9 as appealing for some as scary for others. In any case, CRISPR-Cas9 is worth knowing about, learning more and discussing.

\*

CRISPR is a biotechnological method used to change, delete, replace, or regulate genes of plants or animals, including humans.

There has been similar methods to enable gene modification such as nucleases TALENs or so called “zinc fingers”. CRISPR-Cas9 however surpasses them all. This new tool is easy to learn, quick to proceed, effective and much less expensive which casts an entirely new light on DNA molecule and its modifications.

The chance to modify so easily genes of various organisms has provoked visions of new materials, new drugs (CRISPR antibiotic treatment is under intense scrutiny<sup>1</sup>), new crops, or better access to organs for transplantation<sup>2</sup>.

Narrowing our discussion the use of CRISPR-Cas9 to changes of the human genome, we need to make a clear distinction between two very different DNA interventions:

First; **Somatic Gene Therapy.**

When DNA of somatic cells of tissues and organs is changed, only the individual being treated and his somatic cells will be modified. The modification is not transferred to his offspring. Up to this date, there have been hundreds of clinical trials underway utilizing somatic gene therapies. The hope has been to treat diseases such as certain types of leukemia, hemophilia or Parkinson disease.

Second: **Germline cells modifications.**

This other type of gene therapy is done on germline cells, sperms or eggs. When we modify the DNA of germ cells not only does every nuclear cell of the treated individual contain the change, all his descendants also will carry such modification. Under current rules, no such research on human embryos is allowed.

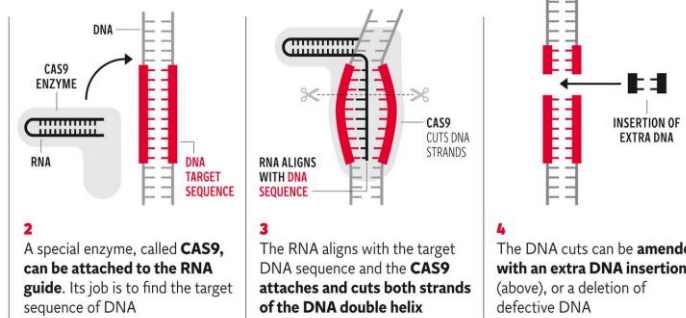
\*

**A BRAVE NEW WORLD OF GENOME EDITING**

How the Crispr system derived from bacteria works on human cells to correct genetic defects



**1** An RNA "guide" molecule can be programmed to match any unique DNA sequence found in the human genome



CRISPR is an abbreviation for “clustered regularly interspaced short palindromic repeats”. Such nucleotide repeats, sequences of non-coding DNA separated by so called spacers, were described in bacteria in 1987<sup>3</sup>. Nobody really knew at that time what such nucleotide palindromes would be good for. Later on, scientists found out that the repeats were an important component of bacterial immunity. When a bacteria encountered a virus or a plasmid, it would incorporate the genetic information of the virus or plasmid into its own, to be able to more readily react on a repeat encounter.

The fact that the immune system is capable to adapting to new threats has been clear since the times of Luis Pasteur. However, it was only in 2012 that the principle learned from bacteria has been shown to have immense possible implications.

The CRISPR method has two components; 1/ a highly precise and effective cellular scalpel, a nucleases Cas9, and 2/ a guide, a RNA molecule that leads the scalpel on a search for a specific nucleotide sequence to be deleted or replaced.

**Figure 2 CRISPR-Cas9 method explained by the [Discovery Zone](#).**

To get a better understanding of the method, see the videos from the two labs and their leading scientists competing for the CRISPR patent; professor

<sup>1</sup> CITORIK, R.J., MIMEE, M., LU, T., K. Sequence-specific antimicrobials using efficiently delivered RNA-guided nucleases. *Nature Biotechnology*, 2014. **32**, pp. 1141-1145. Doi: 10.1038/nbt.3011

<sup>2</sup> SERVICK, K. Gene-editing method revives hopes for transplanting pig organs into people [online]. Published Oct. 11, 2015. [cited Dec 9, 2015]. Available from: <http://news.sciencemag.org/biology/2015/10/gene-editing-method-revives-hopes-transplanting-pig-organs-people>

<sup>3</sup> Ishino, Y. et al. Nucleotide sequence of the iap gene, responsible for alkaline phosphatase isozyme conversion in *Escherichia coli* and identification of the gene product. *Journal of Bacteriology*, 1987. 169 (12). Pp. 5429-5423.



**Jennifer Doudna** from University of California in Berkeley, [Genome Engineering with CRISPR-Cas9](#), and professor **Feng Zhang** from Massachusetts Institute of Technology (MIT), [Genome Editing with CRISPR-Cas9](#).

\*

As we mentioned above, CRISPR allows scientists not only to delete or replace a certain gene. Using the method scientists may also regulate any gene in a genome. Activation or inhibition of a certain gene modifies translation of a nucleotide sequence into a RNA molecule, a template for protein synthesis. Moreover, CRISPR could modulate epigenetic level of gene regulation, using e.g. histone modifications <sup>4</sup>

\*

The implications of the new method are concerning. Along with the great power over the heritable information comes a great responsibility for both, our own genome – and of the generations to come – and the genomes of other species that inhabit our planet. The grand challenges and opportunities of genome edition must be discussed across the society. Scientists and bioethicists, medical student and medical doctors, as well as the public should be aware of the developments in the field and debate their risks and benefits.

<sup>4</sup> PETR, J. CRISPR: přesná střelba na genetické cíle. *Vesmír*, 2015. 5 (27).

An international group of scientists met in Washington, D.C. in December 2015 at a conference organized by the National Academy of Science and the Institute of Medicine, and hosted also by the Chinese Academy of Science and the Royal Society of London.

The Chinese participation on the conference was especially important giving the ethically challenging study on – however non-viable – human embryos of a

Chinese research team published in April, 2015.<sup>5</sup>

The group in Washington attempted to seek a moratorium on inheritable human genome edition. “The overriding question is when, if ever, we will want to use gene edition to change human inheritance”, **David Baltimore**, an American biologist, former president of the prestigious California Institute of Technology

and the Nobel Prize laureate said in his opening speech.

Opponents of the current lack of boundaries as to what can be done to the DNA within cells and organisms emphasize the lack of knowledge that is both deep and wide. Jennifer Doudna in her article for the magazine *Nature* in December 2015 called for communication on safety, guidelines and regulation

*„If I consider the problem as that which the world is turning me into – that is, as a tiny screw in a giant machine, deprived of human identity – then there is really nothing I can do. Obviously I cannot put a stop to the destruction of the globe, the growing stupidity of nations and the reproduction of thousands of new thermonuclear bombs. If, however, I consider it as that which each of us originally is, or rather what each of us – irrespective of the state of the world – has the basic potential to become, which is to say an autonomous human being, capable of acting responsibly to and for the world, then of course there is a great deal I can do.“*

Václav Havel:  
Letters to Olga – essays written in prison, letter,  
March 6, 1982

<sup>5</sup> Liang, P. et al. CRISPR/Cas9 –mediated gene editing in human triploid zygotes. *Protein & Cell*, 2015. 6, (5), pp. 363-372.

that should stem from international cooperation of policymakers and scientists, and extreme caution in handling a tool we simply don't know enough about yet.<sup>6</sup>

On the other hand, proponents of more liberal research suggest that one-gene conditions such as Huntington disease or muscle dystrophies that make one's life truly miserable could be easily fixed just by changing one gene or often, such as in case of sickle cell anemia, one letter in a human genome. Prof. **George Church**, a leading member of the team of prof. Feng Zhang, says that "... banning human germline edition could put a damper on the best medical research and instead drive the practices underground to black markets and uncontrolled medical tourism"<sup>7</sup>.

Genes, however, have often more than one effect, and their secondary assignment is often not known. And many conditions "on the list" of the research teams using CRISPR-Cas9 are caused by more than a single gene. Larger modification on the human genome could have unforeseeable outcomes. Thin medical justification, health risk to the future children and also, reinforcing inequality and discrimination in improving human genetic traits are among the commonly raised concerns regarding the method.<sup>8</sup>

CRISPR-Cas9 has been called a revolution in biology, the beginning of a new era and the greatest discovery of the century. Prof. Baltimore and countless other scientists including the inventors of the method, call for extreme caution and widespread discussion on the ethics of human genome edition.

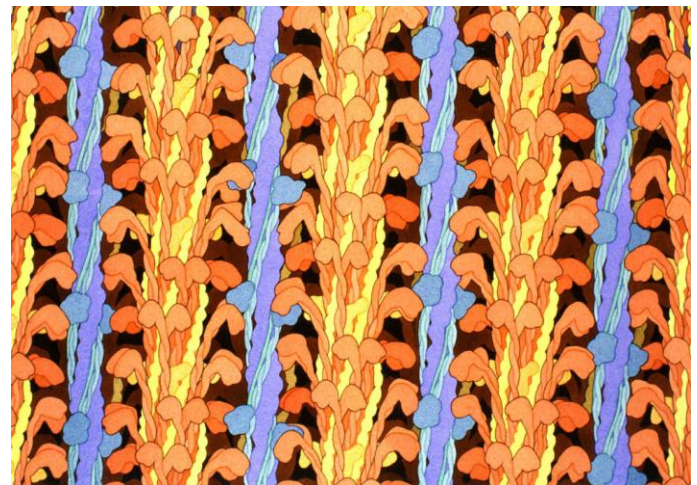
Debates on the use and regulation of CRISPR-Cas9 both in research and clinical practice either of somatic or germline cells has two primary aspects. One aspect is practical; what we can do, change, improve and fix. How advanced is our knowledge and the technologies we use. The other aspect is bioethical; ought we do everything we can? Are the changes and improvements acceptable and desirable? How much is too much for an individual, humankind or any other species on the Earth? Such questions and many more have become pressing in recent months following the discovery of CRISPR-Cas9, and will continue to be controversial topics in the years to come.

\*\*\*

### *Image of the Month*

#### **Sarcomere**

Author: [David S. Goodsell](#) from the [Scripps Research Institute](#) in the California, USA.



**Figure 3 A part of a muscle sarcomere with actin filaments in blue and myosin filaments in red. The long yellow proteins are the huge protein titin.**

\*\*\*

---

<sup>6</sup> Doudna, J. Embryo editing needs scrutiny. *Nature*, 2015. 528, pp. S6.

<sup>7</sup> WADE, N. Scientists Seek Moratorium on Edits to Human Genome That Could be Inherited. *The New York Times*, Dec 3, 2015

---

<sup>8</sup> Center for Genetics and Society. Genetically modified humans? Sever reasons to say no. May, 2015. Available from: [http://geneticsandsociety.org/downloads/7\\_Reasons.html](http://geneticsandsociety.org/downloads/7_Reasons.html)

Series:

## Endocrine Disruptors, part V

### (Re) Introduction

Endocrine disrupting chemicals; even if you have not heard this expression before you surely have read about eggshell thinning of birds of prey, intersex fish, estrogens in tap drinking water and pesticides in veggies, hormones in milk, or even about the, now banned, BPA in plastic bottles for infant formula. Since the term endocrine disruption was coined in 1991 they have been found to be ubiquitous, therefore the subject itself is a bit overwhelming. However, as a medical professional you need to learn about the basic principles of endocrine disruption because it goes far beyond a fertility dysfunction and conception failure.

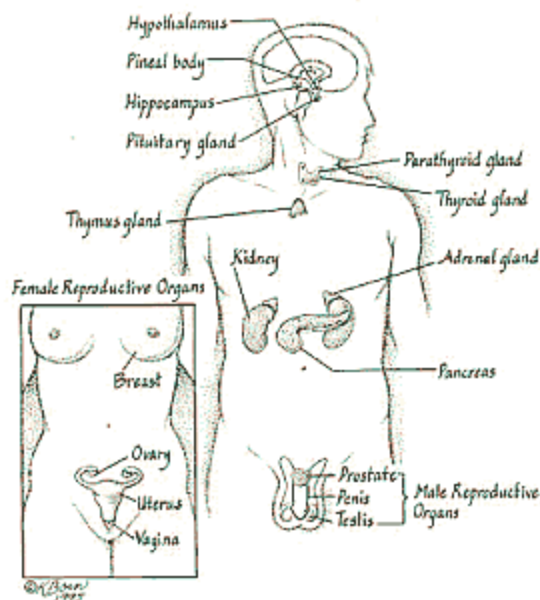


Figure 4 Body organs responsive to the chemical signals.

Source: [TEDX](#)

Let's begin with the fact that cells, tissues and organs do communicate with each other as well as in themselves. The means of their communication in humans are basically two; chemical and electric signals. Here we will put aside electric signaling and speak of chemical communication only. Cellular chemical signals represent tiny molecules, typically hormones and enzymes. Remember the picture from your lectures? Receptor as a lock – and a signal molecule as a key.

Endocrine disruptors are hormonally active molecular compounds in the environment that interfere with the chemically communicating systems in an organism. What body systems? Endocrine,

immune and nervous systems; they all use chemical signalling to communicate within and to control other body functions, including behavior, and intergrate all the functions to work smoothly together.

\*

Example?

*P,p,' DDE is a metabolite of a well known pesticide DDT. DDE is an antiandrogen, meaning it blocks receptors for a body hormone androgen. At the same*

*time, DDE, however weakly, stimulates estrogen receptors. Overall, when in a living organism, DDE has an feminizing impact<sup>9</sup>, i.e. low sperm motility, higher number of defect sperms, smaller male gonades, and in frogs proven ovary occurrence in male individuals.*

\*

Endocrine disruptors interfere with hormonal functions in many ways. EDCs can:

- Act as agonists, mimicking the effect of a natural hormone and binding to its receptors
- Act as antagonist, either preventing the binding of a hormone to its receptor or blocking the hormone's synthesis
- Increase hormone synthesis, hormone elimination or its transportation within the body
- "prime" the organism to be more sensitive to hormones later in life<sup>10</sup>

<sup>9</sup> FRY, D.M., TOONE, C., K. DDT-induced feminization of gull embryos. *Science*, 1981. **213** (4510), pp. 922-924.



### *EDCs during development*

The most concerning aspect of EDCs is their impact during early development. Exposure to exogenous compounds with endocrine disrupting potency before and around birth may result in irreversible adverse outcomes for an individual or even for his/her progeny. The period of time during which a fetus is most sensitive to either functional or structural impairment of tissues or organs is called the “**critical period**”. During the days and weeks of the critical period an organ is extremely prone to disruption in the development its correct structure or function.

\*

### *Example?*

*One of the best studied exogenous compounds is the drug diethylstilbestrol (DES). DES is a synthetic drug first made by Sir Charles Dodds in 1938. Shortly after the WWII it was marketed as a “miracle drug” and prescribed, among others, to pregnant women for preventing premature termination of pregnancies even though studies done in the 1950s showed that DES had no effect on the maintenance of a pregnancy.*

*It is estimated that between 1938 and 1971 over a million fetuses were exposed to DES. The ban came when an unusual tumor was discovered in the reproductive tracts of women whose mothers had taken DES early in their pregnancies. Following studies revealed that more than 95% of females exposed to DES in utero had some abnormalities in the structure of their reproductive organs, and the risk of getting breast cancer increased three-fold<sup>11</sup>. The DES did effect women as well as men, they call*

<sup>10</sup> Ecological Developmental Biology, Gilbert, S.,F., Epel, D. 2009. ISBN 978-0-87893-299-3

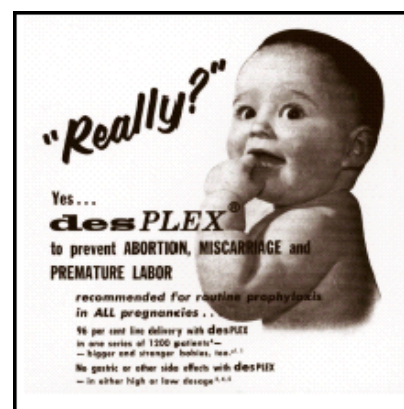
<sup>11</sup> PALMER, J.R. et al. Prenatal DES exposure and risk of breast cancer. *Cancer Epidemiology Biomarkers & Prevention*, 2006. **15**, pp. 1509-1514.

*themselves “DES daughters and sons”. DES was the first documented example of a transplacental carcinogen in humans, and thus proof that **consequences of prenatal exposure may be manifested in adulthood.***

*And we know even more now; most of the changes seen in the DES exposed men and women can be replicated to the next generation. In other words, individuals never exposed to the drug, neither swallowing the pill or in getting it through their mother’s placenta, can experience symptoms of DES exposures (so called **DES granddaughter effect**).*

*The effect we describe as epigenetic inheritance.*

\*



**Figure 5 1956 advertisement promoted the use of of DES aimed at obstetricians**

Endocrine disruptors comprise a complicated group of compounds as they differ in **origin** (natural, e.g. phytoestrogens vs synthetic estrogens), **size** (from kilodaltons to nanometers), **potency** (unlike typical toxins EDCs have a great effect in very low concentration and the traditional saying “the dose makes the poison” does not always apply here), “**life cycle**” (pharmacodynamics of the compounds with endocrine systems disrupting effect is often different from the life cycle expected in traditional drug testing), **dose** and **type of effect** (e.g. estrogenous receptors are ancient and widespread therefore a molecule of estrogen can have a curious effect depending on the receptor, timing and dosage of the drug).

\*

*Do I ever get exposed to EDCs?*

Yes. In fact, all the time. Hormone disrupting chemicals are ubiquitous in our technological society. We inhale them, drink and eat them, we touch them every day. EDCs can be detected in every tissue including breast milk. EDCs are used to soften or harden, or otherwise improve synthetic materials. Possible and proven EDCs are present in plastics and pesticides, phones and personal electronic devices, furniture and cleaning products, shampoo and lipstick, food and food packaging.

\*

*What makes endocrine disruptors different from other chemicals?*

The answer is a summary of what's been written above, and two-fold; dose and timing.

A key feature of endocrine disruptors is their effectiveness in **very low concentrations**.

Moreover, effects in very low concentration can be different from an effects of the same chemical at higher concentration<sup>12</sup>.

**Timing**, on the other hand, is important particularly in early development. During early human development, cells must be present in the right place and receive the right signal in the right strength. If an exogenous chemical mimics signaling out of the right time/dose/place frame, a birth defect may occur. In teratology we talk about so called

“critical periods”, the time during development when an organ or a tissue are gravely sensitive to erroneous stimuli.

\*

Vocabulary:

Endocrine disrupting chemicals, EDCs, endocrine disruptors

- hormonally active substances that interfere with normal signaling in endocrine, immune or nervous systems

DDT, 1,1,1, trichlor-2,2-bis (4chlorfenyl) ethane

- an organochloride
- one of the oldest and most infamous insecticides

DDE,

dichlorodiphenyldichloroethylene

- a chemical compound formed by the loss of hydrogen chloride from DDT

DES, diethylstilbestrol

- synthetic non-steroidal estrogen
- between 1938 and 1971 prescribed to women in pregnancy and menopause, banned in 1971 when shown to

cause cancer in young daughters and sons of exposed pregnant women

- a classified endocrine disruptor

\*\*\*

*When such events happen, there is inevitably a call for the further homogenization of society,; we get rid of the Jews, then Germans, the bourgeoisie, then dissidents, then Slovaks – and who will be next in line? The Roma? Homosexuals? All foreigners? And who will be left? Pure-blooded little Czechs in their own little garden. It's not just that such a position or, ultimately, such a policy is immoral, it's also suicidal.“*

Václav Havel:  
Diary entry for 26 April 2005, To the Castle and Back, 2006

<sup>12</sup> Endocrine society. Endocrine-Disrupting Chemicals. An Endocrine Society scientific statement, 2009. Doi: 10.1210/er.2009-0002.

## Poem of the Month

### Moods

Jack London (October 1898)

Who has not laughed with the skylark,  
    And bid his heart rejoice?  
Laughed till the mirth-loving heavens  
    Echoed his laughter back?  
Joyed in the sheer joy of living,  
    And sung with gladsome voice,  
Lays that were cheerful and merry,  
    And bid his heart rejoice?

Who has not frowned in the gloaming,  
    And felt the skies grow black;  
While o'er him spread the dark mantle  
    Of sullen, solemn Gloom,  
Whose mutterings broke the silence  
    Like echoes from the tomb -  
Like echoes of lost endeavors -  
    Reproaches from the tomb?

Who has not cursed in his passion,  
    As Anger's stinging lash,  
Biting and smarting and racking,  
    Fell on his naked back?  
Felt in his veins feverish tumult,  
    The strife, the savage clash,  
As when hot steel, leaped from the scabbard,  
    Meets steel with crash on crash?

Who has not wept in his sorrow,  
    And looked in vain for morn;  
Waiting with hopeless yearning,  
    The sun from out the bourn?  
Heard from the world the sad sobbing  
    Of Faith and Hope forlorn  
Known that the sun had forever  
    Gone down into the bourn?

## Eponym

### Franz Nissl (1860-1916)



Franz Nissl was a German psychiatrist and neurologist at the turn of the 20<sup>th</sup> century, probably the greatest neuropathologist of his times and an excellent clinician, too. For example, in his practice he made lumbar puncture, a method introduced by his contemporary Heinrich Quincke, a routine diagnostic procedure. In addition to his expertise as a clinician, he dedicated much time to his own research.

Nissl was born in the town of Frankenthal, in southwestern Germany. His father, Theodor, wished little Franz to become a priest and therefore equipped his son with a perfect knowledge of Latin. However Franz Nissl left for Munich to study medicine at the Ludwig Maximilian University. He specialized in psychiatry.

As a final year med student he took part in a research challenge regarding an original piece of work in neurology. Nissl submitted a study based on his own observations and investigations of the cerebral cells of the cortex.

Nissl's professor Bernhard von Gudden, one of the arbitrators of the challenge, was very much impressed with Nissl's work and offered him an internship; an offer Nissl could hardly turn down. Prof. Gudden was a personal physician to the Bavarian king, Ludwig II.

After three year as an assisting professor, Franz Nissl made a move to the University of Frankfurt. There he met and collaborated with excellent minds of his

times, such as German pathologist **Carl Weigert** and the anatomist and neurologist **Ludwig Edinger**. Franz Nissl became close friends with **Alois Alzheimer**, and together they published their histology and histopathology observations of telencephalon in a study *Histologische und histopathologische Arbeiten über die Grosshirnrinde 1904-1921*.

In 1895 Franz Nissl accepted an invitation from the founding father of psychiatry, **Emil Kraepelin**, to become one of his assisting physicians at the University of Heidelberg. During the years to follow, Franz Nissl became a professor and when Kraepelin left for Munich, also a director of the Institute of Psychiatry. After WWI Franz Nissl followed Kraepelin to Munich to perform an exciting psychiatric research. However, in less than one year of intense scientific endeavors Franz Nissl died of kidney failure.

*What is named after Franz Nissl?*

#### **Nissl substance**

Nissl substance are rough endoplasmic reticulum and ribosomes found in neuron bodies and dendrites, rough endoplasmic reticulum

Synonyms: Nissl bodies, Nissl granules, basophil substance, chromaffin substance, tigroid bodies

#### **Nissl degeneration**

Nissl degeneration is such a degeneration of a neuron body that occurs after transection of the axon. Nissl degeneration is characterized by dispersion of the Nissl substance, soma swelling, and the nucleus shifting off the center.

**Nissl stain** is a histology method for staining nerve cells.

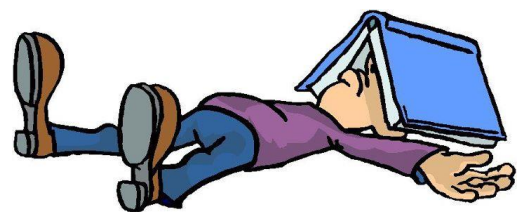
**We wish you**



**2016**

**And**

**Good Luck with your  
Semestrial Examinations!**



The Internal Newsletter, Third Faculty of Medicine, Charles University in Prague.

Editorial Board:

MUDr. Klára Matoušková, MPH – editor

[klara.matouskova@lf3.cuni.cz](mailto:klara.matouskova@lf3.cuni.cz)

MUDr. Lucie Hubičková-Heringová, Ph.D.

MUDr. Eva Maňáková, Ph.D.

Full text available at:

<http://www.lf3.cuni.cz/en/departments/histologie/hep/>