II Международный Симпозиум «Век регенеративной медицины»
II International Symposium «Age of Regenerative Medicine»

по проблемам пролиферации и дифференцировки экто-мезенхимальных стволовых клеток человеческого неба

*in vitro и ex vivo*

on Proliferation and Differentiation of human ecto-mesenchymal Stem Cells from Human Palate evaluated *in vitro and ex vivo*

13 -18. 05. 2015

Hosting organization: Stavropol State Medical University, Russian Federation

Принимающая организация: Ставропольский государственный медицинский университет

Executive Chair: Prof. Dr. W.-D. Grimm

Руководители секций и президиум: Проф. Щетинин Е.В., проф. Гримм В.-Д., проф. Сирак С.В., проф. Аксененко В.А., проф. Д. Видера, Dr. Б. Гиссенхаген, проф. Е.Г. Скурихин.

Session Chairs and Presidium: Prof. E.V. Dr. Shchetinin, Prof. Dr. W.D. Grimm, Prof. Dr. S.V. Sirak, Prof. Dr. V.A. Aksenenko, Prof. Dr. D. Widera, Dr. B. Giesenhagen, Prof. Dr. E.G. Skurikhin

Рабочие языки симпозиума: Английский, Русский.
Working languages: English, Russian


Stavropol
Welcome message Prof. Dr. V.I. Koshel, Acting Rector

Such a massive and representative scientific and practical Symposium, carried out in StSMU second time, and hopefully we can already speak about a new tradition. Video bridge by linking all the parts of both Europe and Asia would allow scientists of the leading colleges and institutions in Russia, Germany and others to present their ideas. What’s more, that is one perfect way to share one’s investigation process with colleagues so improving it’s effectiveness. In addition, the forum is aimed at widening the international cooperation in this dynamically developing sector of medicine.

Nonetheless such arrangements demand the investment of money, knowledge and time spent they claim to be essential for developing new worth-while methods and putting them into practice. Great part of the conference regards young scientists, particulary there’re “young scientist school” and qualification improvement lessons for them held by masters of the case.

Definitely, the Symposium program will be found interesting and usefull for the matter of professional growth by all the participants.
Welcome message Prof. Dr. Grimm, Program committee

On behalf of the Program Committee of StSMU’s II. International Symposion for Regenerative Medicine, it is a great honor to welcome you from all over the world. Here I am honored to declare the II. International Symposion for Regenerative Medicine will be held in Stavropol, Russian Federation during May 13-18, 2015, with a theme of «Age of Regenerative Medicine». Regenerative medicine and stem cell constitute a huge industry of medical technology and services, which is led to the Multi-disciplinary Cross Action and cooperation, such as Basic Sciences, Novel Technologies, and Clinical Translations. Regenerative medicine and stem cell are currently hot subjects of research in today’s life sciences and provide so many promising options for the future treatment of some major disease such as cancer, nervous disease, damaged organs and inflammational diseases. It has a perspective to form a biotechnology industry chain with the development of regenerative medicine industry as the center, which will be one of the high-tech industries with the huge potential in 21st century.

Our event in Stavropol focuses on building a bridge between the researchers in Russian Federation and abroad and will provide all participants with resources, information and advice they might need to aid their research and future professional developments.

Wish you enjoy the conference.

Sincerely Yours
Wolf-Dieter Grimm
Программа симпозиума
Program of the Symposium

14.05.15.
9-00 Регистрация участников. Холл центрального корпуса СтГМУ, Ставрополь, ул. Мира, 310.
Registration of participants. Hall of the StSMU central building, Mira str. 310, Stavropol
10-00 Открытие Симпозиума:
Opening of the Symposium:
Приветственное слово ректора, профессора В.И. Кошель
Welcome message Acting Rector, Professor V.I. Koshel
Приветственное слово проректора по НИР, профессора Щетинина Е.В.
Welcome message Prof. E.V. Shchetinin, Vicerector
10-30 Первое пленарное заседание
10-30 First section
Зал «Звездочка», СтГМУ, Ставрополь, Мира, 310.
Hall «Star», StSMU, Mira str., 310, Stavropol
Заседание 1: Стволовые клетки нервного гребня как инструмент регенеративной медицины
Section I: Neural Crest-Derived Stem Cells as a Tool in Regenerative Medicine

Президиум
Presidium
Проф. Щетинин Е.В., проф. Гримм В.-Д., проф. Сирак С.В., проф. Аксененко В.А., проф. Д. Видера, Dr. Б. Гиссенхаген, проф. Е.Г. Скурихин.
Prof. Dr. E.V. Shchetinin, Prof. Dr. W.D. Grimm, Prof. Dr. S.V. Sirak, Prof. Dr. V.A. Aksenenko, Prof. Dr. D. Widera, Dr. B. Giesenhagen, Prof. Dr. E.G. Skurikhin
10:30-10.40  Исследование: Стволовые клетки гребня как инструмент регенеративной медицины
*Translational Research: Crestal-related Stem Cells as a Tool in Regenerative Medicine*
В.-Д. Гримм
*W.-D. Grimm*

10:40-11.00  Стволовые клетки неврального гребня как инструмент регенеративной стоматологии.
“*Neural Crest-Derived Stem Cells as a Tool in Regenerative Dentistry*”
Д. Видера
*D. Widera*

11:00-11.15  Исследование мультипотентных стволовых клеток в экспериментальном фиброзе. Возможные пути регуляции дифференцировки мультипотентных стволовых клеток.
*Investigation of Mesenchymal Multipotent Stromal Cells in Experimental Fibrosis. Possible Ways of Regulation of the Differentiation of Mesenchymal Multipotent Stromal Cells*
Е.Г. Скурихин, О.В. Першина
*E.G. Skurikhin, O.V. Pershina*

11:15-11.30  Повторное использование медикаментов антиметастатического действия, он-лайн.
*Re-use of established drugs for anti-metastatic indications, on line presentation.*
Ф. Энчладен
*F. Entschladen*

11:30-11.45  Слияние клеток и раковые стволовые клетки, он-лайн.
*Cell Fusion and Cancer Stem Cells, on line presentation.*
Томас Диттмар
*Thomas Dittmar*
11:45-12.00 Мезенхимальные дентальные стволовые клетки как многообещающий инструмент нейрорегенерации, он-лайн.
Mesenchymal stem cells of dental origin as promising tools for neuroregeneration, on line.
Г. Варга
G. Varga

12:00-12.15 Сравнительный анализ мезенхимальных стволовых клеток изолированных из пульпы и периодонтальной связки. он-лайн.
Comparison of Mesenchymal Stem Cells Isolated From Pulp and Periodontal Ligament, on line presentation.
Сема С. Хакки
Sema S. Hakki

12:15-12.30 Организация центра регенеративной медицины на базе Банка стволовых клеток Покровска. Он-лайн.
Centre of Regenerative Medicine Organization on the Basis of Pokrovskij Stem Cell Bank. On line.
Д. Иволгин, А.Б. Смольянинов
D. Ivolgin, A.B. Smolyaninov

Дискуссия

12-40 Кофе-брейк
Coffee-breake

13-00 Второе пленарное заседание
Secound section.
Зал «Звездочка», СтГМУ, Ставрополь, Мира, 310.
Hall «Star», StSMU, Mira str., 310, Stavropol.

Тема заседания: Изоляция и дифференцировка экто-мезенхимальных стволовых клеток неба для регенеративных процедур в стоматологии
Topic of the section: Isolation and Differentiation of Crestal-related palate-
derived ecto-mesenchymal Stem Cells for Regenerative Procedures in Dentistry

Президиум
Проф. Щетинин Е.В., проф. Гримм В.-Д., проф. Сирак С.В., проф. Аксененко В.А., проф. Д. Видера, Dr. Б. Гиссенхаген, проф. Е.Г. Скурихин.
Prof. Dr. E.V. Shchetinin, Prof. Dr. W.D. Grimm, Prof. Dr. S.V. Sirak, Prof. Dr. V.A. Aksenenko, Prof. Dr. D. Widera, Dr. B. Giesenhagen, Prof. Dr. E.G. Skurikhin

13:00-13.45 Аллогенные заменители человеческой кости – клинические результаты метода костных колец.
*Human allogen bone substitutes – Clinical Results of the Bone-Ring Method*
Б. Гиссенхаген
*B. Giesenhagen*

*Translational Research: Crestal-related ecto-mesenchymal Stem Cells from Human Palate: A New Hope for Alveolar Bone and Cranio-Facial Bone Reconstruction-Clinical Results*
В.-Д. Гримм, Б. Гиссенхаген, Е.В. Щетинин, Д. Видера, С.В. Сирак
*W.-D. Grimm, B. Giesenhagen, E.V. Schetinin, D. Videra, S.V. Sirak*

14:10-14.30 Трехлетний результат латеральной аугментации с использованием аллогенных костных блоков перед имплантационной стоматологией. Он-лайн
*Three year results of lateral augmentations using human allogen bone blocks before implant dentistry. On-line*
И. Счау, В.Д. Гримм
*I. Schau, W.-D. Grimm*
14:30-14.45 Activation and migration of CD4+ lymphocytes induced by different “foreign bodies”

D.V. Bobryshev, S.V. Sirak, O.V. Vladimirova, W.-D. Grimm

14:45-15.00 The influence of porous titanium for the osteogenic potential of bone marrow cells in vitro and in vivo

S.V. Sirak, W.-D. Grimm

15:00-15.15 3D reconstruction of non removable implant supraconstructions in ceramics. On-line

M.A. Vukovic, W.-D. Grimm

15.15-15.30 Conical implant systems support alveolar bone regenerative processes.

R. Donaca, chair, Argon Dental - part of Argon Group, Germany

15.30-14.00 Biological scaffolds creation of rat’s and nonhuman primate intrathoracic organs and tissue

Позднее итоги симпозиума

*Summary of the symposium*

Профессор В.Д. Гримм, СтГМУ, Ставрополь, Россия, Виттен/Хердеке Университет, Германия

*Prof. W.-D. Grimm, Stavropol State Medical University, Stavropol, Russia, Witten/Herdecke University, Germany*

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*G. Varga, Prof. Dr., Semmelweis University Budapest, Hungary*

Профессор Д. Видера, Университет Ридинга, Великобритания

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*B. Giesenhagen, Dr., University of Frankfurt/M., Germany, Implant Center Kassel, Germany*

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International Research, Clinical and Education Center of Regenerative Medicine, Kuban State Medical University, Krasnodar, Russian Federation
Biological scaffolds creation of rat’s and nonhuman primate intrathoracic organs and tissue

Проф. Томас Диттмар, Институт иммунологии и экспериментальной онкологии, Центр Биомедицинского образования и исследований, Виттен/Хердеке Университет, Германия
Thomas Dittmar, Prof., Institute of Immunology & Experimental Oncology, Center for Biomedical Education and Research (ZBAF), Witten/Herdecke University, Germany

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Dmitry Ivolgin, Prof. Dr. A.B. Smolyaninov, 1 North-Western State Medical University n.a. I.I. Mechnikov, Pokrovskij Stem Cell Bank

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E.V. Shchetinin, Prof. Dr., Vicerector, Stavropol State Medical University, Stavropol, Russia
II. Международный Симпозиум «Век регенеративной медицины»
II. International Symposium «Age of Regenerative Medicine»

по проблемам пролиферации и дифференцировки экто-мезенхимальных стволовых клеток человеческого неба in vitro и ex vivo

on Proliferation and Differentiation of human ecto-mesenchymal Stem Cells from Human Palate evaluated in vitro and ex vivo

14.05.15
Abstract

Neural crest cells (NCC) are migratory multipotent cells that give rise to diverse derivatives. NCC respond to various environmental factors throughout their development, including bone morphogenetic proteins, epidermal growth factor (EGF), Wnt proteins, stem cell factor, and endothelin 3 (EDN3) (Lee et al., 2004; Shah & Anderson, 1997), and differentiate into many cell types, including neurons and glial cells of the peripheral sensory and autonomic ganglia, Schwann cells, melanocytes, endocrine cells, smooth muscle, and skeletal and connective tissue cells of the craniofacial complex (Le Douarin & Kalcheim, 1999).

NCC emerge from the dorsal edge of the neural folds, delaminate from the surrounding tissues of the fusing neural tube, and then migrate throughout the embryo. In the trunk, NCC exit dorsally from a closed dorsal neural tube (Milet & Monsoro-Burq, 2012) and migrate along two major routes:
- the ventromedial pathway between the neural tube and somites, along which NCC give rise to the autonomic ganglia (sympathetic ganglia and parasympathetic ganglia), dorsal root ganglia (DRG), glial cells, and chromaffin cells;
- and a dorsolateral pathway between the overlying ectoderm and somites, along which NCC give rise to melanocytes (Le Douarin & Kalcheim, 1999; Le Douarin & Teillet, 1974).

NCC maintained their multipotency after emerging from the neural tube.

A major limitation in the study of neural stem cells has been the inability to identify them prospectively in vivo. This is because there have been no markers to isolate the stem cells or to distinguish them from restricted progenitors in vivo. Thus, multipotent, self-renewing neural stem cells have all been isolated after a period of growth in culture that could change their properties. It is therefore not yet clear whether such cells derive from cells with similar properties in vivo.

In our studies we identified cells positive for the neural stem cell/neural crest-specific intermediate filament nestin adjacent to Meissner corpuscles and Merkel cell-neurite complexes within palatal ridges (palatal rugae/rugae palatinae). These cells were characterized by expression of nestin, the transcription factor Sox2, and additional neural crest markers such as Slug or Snail.

In their target tissues, the uncommitted neural crest cells differentiate into cells of both mesodermal and ectodermal type, giving the neural crest its description
as a probable fourth germ layer. Growth factors and the specific microenvironment in target tissues seem to be important for neural crest differentiation, as neural crest cells have been shown to change their properties when transplanted into different tissues during development. NCSC-like cells have also been identified in the palatum and periodontal ligament through a sphere-forming culture system that was originally utilized to isolate neuronal stem cells (Widera et al., 2007, 2009, Grimm et al. 2011, 2014, 2015, Keeve et al. 2012).

**Biography**

Wolf-Dieter Grimm, clinical periodontist, graduated from dentistry, St. Peterburg State University in 1968. He worked for Technical University Dresden, for Academy of Postgraduate Programs in Dentistry Schwerin, and Witten/Herdecke University, Faculty of Health, Germany since 1991 to date. Since 1992, he became the Chairman of Department of Periodontology, Faculty of Dental Medicine, University of Witten and the director of Dental clinics 1993-97. From 1997-2005, he worked in USA as an Adjunct Professor in the Department of Periodontology, University of North Carolina at Chapel Hill. As Professor of Periodontology he has decades of experience with the diagnostic and treatment of periodontal diseases.

As PI Prof. Grimm has developed rodent (rat and mice) animal models including animal experimental surgery (titanium chamber model); histological techniques (organ/tissue/cell isolation, fixation, processing for light/scanning electron microscopy, embedding, sectioning, specific/differential staining) and radioactive labeling in vivo/in vitro, autoradiography for the investigation of periodontal regeneration. Since 2006 he focused on the Stem cells in Advanced Regenerative Periodontology and Dental Implantology and got some important success. In standardized animal model, he can investigate periodontal and alveolar bone regeneration in nude rat. Nowadays he and his clinical team is developing new techniques for vertical and horizontal augmentations of alveolar bone defects using human allogenic bone substitutes as carrier material for human ecto-mesenchymal stem cell-enriched palatal-derived tissues in patients. Prof. Grimm has been awarded three times with the Colgate-Research Award. Since 2010 Prof. Grimm is running a privat practice “Praxisteam Hasslinghausen” specialized on Advanced Periodontology and Dental Implantology in cooperation with Dr. M.A. Vukovic. Since September 2014 Prof. Grimm is additionally working as Distinguished Gottfried Herder Exchange Program Professor of Stomatology (Germany) at Stavropol State Medical University (Russian Federation).
Abstract

The embryonic neural crest appears during development of mammals including humans as a transient structure between the newly formed ectoderm and the neural tube. Due to their intrinsic ability to give rise to mesenchymal and ectodermal derivatives, neural crest stem cells possess an extraordinarily high developmental potential surpassed only by totipotent cells of the zygote and pluripotent embryonic stem cells. Adult neural crest-derived stem cells (NCSCs) were long-term believed to be an in vitro phenomenon similar to embryonic stem cells derived from the inner cell mass of a blastocyst. During the last 15 years, however, an emerging line of evidence supported the hypothesis that at least a limited number of adult NCSCs may exist in the human body even in adulthood. Remarkably, such adult NCSCs perform self-renewal and exhibit a differentiation potential comparable to their embryonic counterparts. In particular, they can give rise to neurons, melanocytes, bone cells, and cartilage in addition to many cell types associated with tooth development and homeostasis.

Biography

11.2012 Habilitation (German professorial qualification) and “venia legendi” for Cell Biology at the University of Bielefeld, Faculty of Biology, Germany. Habilitation-Thesis: “Alternative sources of adult stem cells for neuronal regeneration and the role of NF-kB in endogenous neural stem cells and neurons”

07.2007 Dr. rer. nat. (PhD) in Neurobiochemistry at the Institute for Neurobiochemistry (Kaltschmidt Lab), Witten/Herdecke University, Germany. Grade: summa cum laude (with distinction)


11.2004 Diploma in Biochemistry (Dipl. Biochem.) at the Witten/Herdecke University, Germany. Grade: 1,0 (A)

Diploma Thesis at the Institute for Neurobiochemistry: “MCP-1 induces migration of adult neural stem cells”

10.2002 Intermediate diploma in Biology at the University Cologne, Germany.
Investigation of Mesenchymal Multipotent Stromal Cells in Experimental Fibrosis. Possible Ways of Regulation of the Differentiation of Mesenchymal Multipotent Stromal Cells

Evgenii Skurikhin, Olga Pershina, Natalia Ermakova, Vyacheslav Krupin, Inna Stepanova, Angelina Pakhomova and Alexander Dygai

Abstract

There is a certain gap in understanding the mechanism of collagen-producing cells rising in lung parenchyma – fibroblasts. It is known that bone marrow, circulating in blood; adipose tissue-derived mesenchymal multipotent stromal cells (MMSC) differentiate under certain conditions into the stromal cell lineages, including fibroblasts. We investigated distribution and properties of MMSCs, progenitor fibroblast cells in various tissues and organs (bone marrow, blood and lung) from adult mice with pneumofibrosis. In addition, we evaluated in vitro the effect of adrenergic, dopamine and serotonin receptors agonists on MMSCs. The number of adherent mononuclear cells with mesenchymal phenotype (CD31-, CD34-, CD45-, CD44+, CD73+, CD90+, CD106+) after bleomycin injury of alveolar epithelial increased in the bone marrow, blood and lungs of mice. We evaluated the ability of MMSCs and progenitor cells to self-maintenance, clonal activity and differentiation at the long-term cultivation (3 month). We investigated multilineage differentiation potential (osteocyte, adipocyte, chondrocyte and fibrocytes) cells with MMSC-like phenotype. Agonists of adrenergic, dopamine and serotonin receptors affected on the differentiation of MMSCs in vitro. We believe the investigated lung cells can be mesenchymal multipotent stromal cells. Our data showed the consistent activation of MMSCs in the bone marrow and their possible subsequent migration to the lungs, where they participate in the fibrotic changes in the parenchyma.

Biography

Dr. Evgenii Skurikhin now is a professor of Pathological Physiology and Chief of research team by Laboratory of Pathological Physiology and Experimental Therapy from the Research Institute of Pharmacology and Regenerative Medicine named after E.D. Goldberg (Tomsk). He got his Medicine Doctor's degree (Ph.D.) at the Institute of Pharmacology of RAMS SD (2004), Member of the Society of Pathophysiology RU, Member of the Society of Pharmacology RU, Member of the Society of Regenerative Medicine RU and Member of the Dissertation Council of the Institute of Pharmacology. He is Specialist in regenerative medicine. His works were supported by RFFI Grant 00-04-48745 (2000-
2002), MAS Grant 01-04-06153 (2001), project by Regional contest targeted basic research "The Study by stimulation and mobilization of endogenous stem cells as the basis for creating a new process for the production of cellular material for transplantation" (2008). He studies endogenous stem cells and progenitor cells role in the pathogenesis of myelosuppression, idiopathic fibrosis of lung, neurosis, diabetes mellitus 1 and breast cancer, monoamines and system of blood. He headed seven scientific works. He published 7 books (2 on English), 91 articles, has 19 Patent RU.
Abstract
The development process of a new drug from target identification to approval is time-consuming and expensive in any type of indication. Therefore, when a drug once is approved and turns out to be well-tolerated and effective, it is mandatory to further explore the profile of safety and action. On the one hand, possible risks of unwanted side effects have to be monitored in order to protect the patients. On the other hand, there may be some beneficial effects aside from the primary indication, which can only be detected under certain circumstances, e.g. in special subgroups of patients, combination with other drugs or long-term use. These beneficial effects maximize the profit for both patients and companies. This issue of drug repositioning especially applies to the oncological field, since the success rate for new drugs is particularly low as compared to non-oncological indications. Especially the use of newly developed test methods can reveal additional effects that have not been detected before. For example, by means of our cell migration assay we have provided evidence that beta-blockers, which are in clinical use for the treatment of cardiovascular diseases, have an anti-metastatic function. Further, already approved substances may have such an effect. These substances and potentials will be discussed.

Biography
MetaVi Labs is the first company wholly dedicated to stopping metastasis formation. Our 3D collagen-based Preclinical Antimetastasis Screening System (PASS) is the only validated method on the market, from in vitro, to in vivo, to the clinic. This is backed by nine retrospective clinical trials with beta-blockers in 5 tumor types, including melanoma, ovary, lung, breast and colon carcinoma.
Led by Prof. Frank Entschladen, our experts have more than 20 years of research experience in cell migration and oncology. With this revolutionary technology, MetaVi Labs has defined the new standard for pre-clinical antimetastasis screening.
We are actively seeking out-licensing opportunities as well as drug-discovery and companion-diagnostic co-development projects for anti-metastatic agents.
Cell Fusion and Cancer Stem Cells, on line presentation

Institute of Immunology & Experimental Oncology, Center for Biomedical Education and Research (ZBAF), Witten/Herdecke University, Stockumer Str. 10, 58448 Witten, Germany

Abstract

It is well recognized that the biological phenomenon of cell fusion plays a mandatory role in various physiological events, like fertilization, placentation, muscle fiber formation as well as wound healing and tissue regeneration, and pathophysiological processes, including cancer. Here, it is assumed that cell fusion may promote tumor progression due to generation of hybrid cells, which could exhibit novel properties such as an enhanced metastatogenic capacity, and increased drug resistance or a decreased apoptosis rate. Thereby, cell fusion events could occur between tumor cells themselves as well as tumor cells and normal cells, including macrophages, fibroblasts, epithelial cells, or stem (-like) cells. The reason why hybrid cells could be phenotypically different in relation to their parental cells is not yet fully understood, but is most likely attributed to the merging of the nuclei of the parental cells causing chromosomal instability being characterized by translocations, deletions, amplifications and even loss of entire chromosomes. This so-called heterokaryon-to-synkaryon transition (fusion of two parental nuclei to give rise to one hybrid nucleus) is a random, unpredictable process and because of that the ultimate phenotype of the emerging hybrid cells cannot be predicted. The finding that tumor hybrid cells may exhibit an increased metastatogenic capacity suggest that these cells must exhibit cancer stem cell properties since, per definition, only cancer stem cells (or cancer initiating cells) are capable to induce tumor formation, which not only accounts for the primary tumor, but also for secondary lesions, or in other words metastases, at distant organ sites. In this context, we have postulated the existence of so-called recurrent cancer stem cells (rCSCs), which will induce the regrowth of tumors after therapy exhibiting an oncogenic resistance phenotype being characterized by an increased malignancy and resistance against first line therapy. Cell fusion is an ideal mechanism explaining the origin of rCSCs since inflammation and proliferation, which is a common phenomenon in cancerous tissues, is a well-known trigger for the merging of two cells. Moreover, if such fusion events will occur during cancer therapy, the applied chemotherapeutic compounds and/ or radiation will be a good selection pressure for the origin of cancer therapy resistant cancer hybrid stem cells.
Biography
Curriculum vitae
Name Thomas Dittmar, Prof. Dr. (Ph.D.)
Date of birth May 21st 1969
Nationality German
Education/ Positions
1990 – 1995 Studies of Chemistry, Ruhr-University Bochum
1995 Diploma in Chemistry, Ruhr-University Bochum
1995 – 1999 PhD student, Institute of Immunology, Witten/Herdecke University
1999 PhD thesis, Witten/Herdecke University
1999 – 2003 PostDoc, Institute of Immunology, Witten/Herdecke University
2003 – 2009 Juniorprofessor of Tumorimmunology,
Group leader Research Group “Stem Cells”
2009 - 2010 apl. Professor, Witten/Herdecke University
Group leader Research Group “Stem Cells”
2010 - University Professor, Witten/Herdecke University
Group leader Research Group “Stem Cells”
Mesenchymal stem cells of dental origin as promising tools for neuroregeneration, on line presentation

Abstract
Periodontitis is a chronic inflammatory disease leading to alveolar bone destruction, and eventually tooth loss. In genetically or environmentally predisposed individuals periodontopathogenic bacteria trigger an inflammatory immune response where activated macrophages secrete inflammatory cytokines and T helper 17 cells produce interleukin-17, receptor activator of nuclear factor kappa B ligand (RANKL) and tumor necrosis factor-a. Inflammation and the production of RANKL, the key cytokine responsible for osteoclast activation, cause excessive activation of osteoclasts. This results in a decoupling between bone formation and resorption, leading to bone loss. As conventional treatment does not target the inflammatory response and osteoclast activation, its effectiveness is limited. Novel treatments are thus required if we are to cure this disease. Mesenchymal stem cells (MSCs), including those of dental origin, are potent immunomodulators and are known to be suitable for tissue regeneration. MSCs can inhibit the immune response by suppressing T cells, inducing regulatory T cells and converting dendritic cells and macrophages into a regulatory phenotype. Additionally, genetic modulation may enhance the therapeutic potential of MSCs. In the present review the authors describe the potential use of MSCs, either unmodified or engineered for therapeutic purposes in periodontitis, with special emphasis on MSCs from dental pulp and periodontal ligament. The paper envisions that multiple targeting of this inflammatory disease by modulating the immune response, promoting bone regeneration and inhibiting bone resorption might yield significantly improved treatment outcomes when combined with conventional treatment modalities.

Biography
Director. Professor Gábor Varga, Ph.D., D.Sc.
The Department of Oral Biology is the only theoretical/pre-clinical institute of the Faculty of Dentistry. Founded in 1989, the Department was preceded by the Oral Biology Group of the Faculty of Dentistry, which had been formed by staff members of the Department of Pathophysiology with doctoral degrees in dentistry.
Profile: Oral biology deals with the function and interactions of organs functionally related to the oral cavity, and the relationship of these organs with other parts of the organism both in health and disease.
Education: The Department teaches two subjects and several special courses to 3rd, 4th and 5th year dental students: General and Oral Pathophysiology, a pre-
clinical subject with special attention to topics important for dental students, and Oral Biology, which provides knowledge at the pre-clinical level. This latter subject started to be introduced as part of dental education in Hungarian medical schools at the end of the 1970s (1982 at Semmelweis University). The theoretical and practical components of the subjects were developed by the Department’s faculty members, based on the British and Scandinavian approach. Oral biology has been taught in a partial credit-point system since 1994.


Research: The Department’s main focus is on topics related to the interface between modern biology and clinical dentistry. Some of these include:
Postnatal stem cells of dental origin. We isolate cells from human dental pulp and periodontal ligament, to develop in vitro model systems and processes for identification of stem cells, which have the potential for full or partial regeneration of dental tissues. Cultures containing pluripotent postnatal stem cells from the dental pulp (DPSC), from deciduous pulp (SHED) and periodontal ligament (PDLSC) are prepared. We determine their proliferative capacity and clonogenity, and study the effect of BMPs and extracellular matrix components on proliferation and (trans)differentiation of these cultures.

Human salivary gland model for exploring the molecular mechanisms of epithelial secretion and for developing gene delivery techniques. Primary cultures are prepared of human submandibular gland to provide optimal conditions for the formation of either ductal- or acinar-like polarised epithelia. We use cell lines as reference systems. The HSG cells are capable of ductal-acinar transdifferentiation but it does not form a tight epithelial monolayer. Par-C10, Capan-1, Panc-1 and HPAF can form high-resistance epithelia capable of transepithelial electrolyte and water transport. The work helps to establish the basis for future gene therapeutic interventions by pinpointing possible target genes to correct salivary gland dysfunction.

Polymorphism studies of genes potentially involved in periodontitis and hypodontia. The purpose is to map single nucleotide polymorphisms (SNP) related to these disorders in the Hungarian population. Besides polymorphism of genes that are already implicated as factors involved in periodontitis and hypodontia, new SNPs are identified that have not been previously considered as hazards for oral health. These observations may lead to the development of new diagnostic strategies and provide novel tools for early detection and primary control.
Comparison of Mesenchymal Stem Cells Isolated From Pulp and Periodontal Ligament, on line presentation

Abstract

Cell-based therapy using mesenchymal stem cells (MSCs) seems promising to obtain regeneration of dental tissues. A comparison of tissue sources, including periodontal ligament (PDL) versus pulp (P), could provide critical information to select an appropriate MSC population for designing predictable regenerative therapies. The purpose of this study is to compare the proliferation and stemness and the MSC-specific and mineralized tissue-specific gene expression of P-MSCs and PDL-MSCs.

METHODS: MSCs were obtained from PDL and P tissue of premolars (n = 3) extracted for orthodontic reasons. MSC proliferation was evaluated using a real-time cell analyzer for 160 hours. Telomerase activity was evaluated by a telomeric repeat amplification protocol assay based on enzyme-linked immunosorbent assay. Total RNA was isolated from the MSCs on day 3. A polymerase chain reaction (PCR) array was used to compare the expression of MSC-specific genes. The expression of mineralized tissue-associated genes, including Type I collagen (COL I), runt-related transcription factor 2 (RunX2), bone sialoprotein (BSP), and osteocalcin (OCN) messenger RNA (mRNA), was evaluated using quantitative real-time PCR.

RESULTS: Higher proliferation potential and telomerase activity were observed in the P-MSCs compared to PDL-MSCs of premolar teeth. Fourteen of 84 genes related to MSCs were expressed differently in the PDL-MSCs versus the P-MSCs. The expressions of bone morphogenetic protein 2 (BMP2) and BMP6; sex-determining region Y-box 9 (SOX9); integrin, alpha 6 (ITGA6); melanoma cell adhesion molecule (MCAM); phosphatidylinositol glycan anchor biosynthesis, class S (PIGS); prominin 1 (PROM1); ribosomal protein L13A (RPL13A); and microphthalmia-associated transcription factor (MITF) were higher in the P-MSCs compared to the PDL-MSCs, and higher expression of matrix metalloproteinase 2 (MMP2), interleukin (IL)-6, insulin (INS), alanyl (membrane) aminopeptidase (ANPEP), and IL-10 were observed in the PDL-MSCs. However, there was no statistically significant difference in the expression of mineralized tissue-associated genes, including BSP and RunX2, between the P-MSCs and the PDL-MSCs. Higher expression of COL I and lower expression of OCN mRNA transcripts were noted in the PDL-MSCs compared to the P-MSCs.

CONCLUSIONS: The results of this study suggest that MSCs isolated from P and PDL tissues show different cellular behavior. To increase the predictability
of MSC-based regenerative treatment, differences in dental tissue-derived MSCs and favorable aspects of cell sources should be further clarified.

**Biography**
May 2002–present  Professor (Full) Selcuk University • Faculty of Dentistry, Department of Periodontology Turkey • Konya
Research Experience: Periodontics, Cell Adhesion, Cell Biology, Cell Culture, PCR, Gingivitis, Molecular Biology, Periodontal Surgery, Fibroblast, Cell Migration, Periodontal Regeneration, Chronic Periodontitis
Centre of Regenerative Medicine Organization on the Basis of Pokrovskij Stem Cell Bank

Abstract
Pokrovskij Stem Cell Bank began its activity in 2008 as private umbilical cord blood bank. From the very beginning it worked as a hybrid bank as it collected, processed cord blood units both for public and private storage. During this time we managed to create well-skilled team, organized all processes and activities of all bank facilities according to state and international requirements.

In 2011 for a score of reasons both internal and external it was decided to restructure the Bank’s activity. This restructurisation resulted in four areas of focus: cord blood bank (hybrid model), cell cultures facility, molecular genetic laboratory and quality control facility.

UCB bank: main task- organizing the activities in order to collect umbilical cord blood units which can be effectively administer in the field of regenerative medicine. For that purpose we use three methods of umbilical cord blood processing - double centrifugation (manual method), semi-automated and automated stem cells separation. Thus we processed and cryopreserved more than 6000 umbilical cord blood units with high total nuclear cells count.

Molecular genetic laboratory: main tasks – non-invasive prenatal diagnostics (sex and Rh-factor determination of fetus), molecular-genetic testing. This laboratory uses a complex of methods- MLPA, PCR, sequence analysis which allows it to diagnose a wide range of diseases.

Cell cultures facility: main tasks are 1) MSC isolation and expansion techniques (from BM, adipose tissue, UC, UCB); 2) HSC isolation technique from UC; 3) HSC expansion techniques; 4) Investigation of MSC immunomodulatory effects; 5) MSC for traumatology and orthopedyx; 6) Fibroblasts for cosmetology and burns treatment. Haemopoietic stem cells expansion techniques resulted in more than 200 fold increasing of CD34+ count. Mesenchimal stromal cells isolated from various sources (bone marrow, adipose tissue, umbilical cord tissue), expanded in the laboratory are applied in several clinical research protocols- traumatology, autoimmune diseases, regenerative medicine (toxic hepatitis). Fibroblasts administration for burns treatment resulted in two-fold reduction of epithelialization duration of II - IIIa - IIIb grade burn lesions.

Conclusions:
- Through its existence Pokrovskiy SCB developed and established operation algorithms, which allow to receive the cell products that meet standards including international.
- Starting as a small commercial project, Pokrovskiy SCB managed to expand the range of services provided in the result of diversification of activities.
Now Pokrovsky SCB can translate the results of researches in the field of regenerative medicine, including its own, to clinical application of different types of cells.

**Biography**
Dr. Dmitry Ivolgin, Medicine Doctor (Ph.D.-medicine), now is an Senior Researcher in North-West State Medical University Scientific Research Laboratory of Cell Technologies, Medical Director and head of the Cells processing and cryopreservation facility of Pokrovskij Stem cell bank. Specialist in transfusion medicine, haematology, Medicine Doctor’s degree (Ph. D) at Russian Institute of Haematology and Transfusiology. Dr. Dmitry Ivolgin researches focus on all aspects of cells banking activities, especially stem cells processing and cryostorage, an application of perinatal stem cell (mainly non-haematologic) in the field of regenerative medicine is among his research interests.
13:00-13.45: Б. Гиссенхаген, Университет Франкфурта-на-Майне, Германия, Центр Имплантологии Касселя, Германия
Bernd Giesenhagen, Dr., Privat Clinic for Implantology in Kassel, Germany, Johann Wolfgang Goethe University Frankfurt/Main, Germany

Аллогенные заменители человеческой кости – клинические результаты метода костных колец.

Human allogen bone substitutes – Clinical Results of the Bone-Ring Method

Abstract

In the case of advanced atrophy or jaw defects, extensive vertical bone augmentation is often unavoidable to enable patients to be fitted with implants. These implantological procedures are usually two-stage and are very time-consuming for patients. The method of grafting bone rings developed by Berhard Giesenhagen in 2004 makes it possible to augment the bone and insert implants in one single session. There are virtually no limitations to the indications for applying this technique. Compared with the classic, two-stage augmentation using bone blocks, the bone ring technique shortens the overall treatment time by several months. The method will be clearly and graphically presented in a multiple-part series of individual patient cases with the aid of various case studies. If the recommended treatment protocol is followed and the anatomically risk-prone regions are respected, bone grafting and implant placement can be safely performed by the ring technique.

As well as the chin, the palate, the retromolar region and human allogen ring grafts may be considered as donor sites for the ring technique.

Harvesting from these regions and using human allogen ring grafts as well as risks in soft tissue management (incision direction, suturing techniques) will be presented and discussed in the presentation.

The conditions required for successful application of the bone ring technique, in terms of achieving a restoration with long-term stability, will also be explained.

Biography

1980-2011 - Dental practice in Melsungen.
1996 - Medical Director PRO-IMPLANT, Institute for Implantology and Education: Academic partner of Johann Wolfgang Goethe University Frankfurt/Main.
Since many years involved in different educational programs in Germany and abroad.
- Developer of the Bone Ring Technique.
- Well known specialist for augmentation of hard and soft tissue around the world.
- Numerous publications about augmentation and Bone Ring Technique.
2012 - Privat Clinic for Implantology in Kassel
Several recent studies showed that neural crest-related stem cells can be isolated from mammalian craniofacial tissues such as periodontal ligament, dental pulp, and palate. These cells have in common that they form neurosphere-like clusters and proliferate in serum-free culture in the presence of fibroblast growth factor-2 (FGF-2) and epidermal growth factor (EGF). Attempts to regenerate the complex system of tooth-supporting apparatus (i.e., the periodontal ligament, alveolar bone and root cementum) have made progress recently and provide a useful experimental model for the evaluation of future regenerative therapies. Concentrated efforts have now moved from the use of guided tissue/bone regeneration technology, a variety of growth factors and various bone grafts/substitutes toward the design and practice of endogenous regenerative technology by recruitment of host cells (cell homing) or stem cell-based therapeutics by transplantation of outside cells to enhance dental tissue regeneration and its biomechanical integration. This shift is driven by the general inability of conventional therapies to deliver satisfactory outcomes, particularly in cases where the disease has caused large tissue defects. Cell homing and cell transplantation are both scientifically meritorious approaches that show promise to completely and reliably reconstitute all tissue and connections damaged through dental diseases, and hence research into both directions should continue. In view of regeneration of dental tissues this presentation specifically explores and analyses the stem cell types and cell delivery strategies that have been or have the potential to be used as therapeutics in dental tissue regenerative medicine, that may eventually enter into the clinic.

From this perspective, the human palate has been shown to be of critical importance in the regenerative process in dental-alveolar surgery. Our research group describes a new way to prepare the endogenous repairing stem cells on the basis of their ecto-mesenchymal like phenotype (Molthera; PCT/EP2006/066221). Our new cell therapeutic product is already developed on a research laboratory scale. The patient-specific adult stem cells can be easily isolated and propagated without human serum from the palate. Our group gained clinical experience with the bone block technique and isolation, cultivation, and characterization of palate-derived stem cells (paldSCs). Based on this key discovery we developed a regenerative cell therapy.
Three year results of lateral augmentations using human allogen bone blocks before implant dentistry

Abstract

Purpose: Allogenic bone blocks may be utilized as an alternative pre-implantological augmentation procedure for the reconstruction of deficient alveolar bone in cases, in which the transplantation of autogenous bone is impossible or not desired. The present study investigates radiologically detectable changes of peri-implant bone level around dental implants placed into allogenic bone-block augmentations compared to implants placed into non-augmented bone.

Material and methods: 14 patients of the study-group received 40 allogenic bone-blocks and 60 implants in both, maxilla and mandible in a two-step approach. The human study was approved by the ethics-commission of the Wilhelms-Universität Münster, Germany. Radiologic examinations were carried out directly after implant insertion, after prosthetic restoration plus one and three years after prosthetic loading. All radiographs were digitalized, calibrated and measured computer-assisted.

The control group contained 14 patients who had received 53 implants without augmentation. Data of the two groups were compared statistically, using the non-parametric Wilcoxon-test ($\alpha=0.05/4=0.0125$). The two primary end-points of the study were defined as total bone loss 3 years after prosthetic loading and bone loss in the years 2 and 3 after prosthetic loading. Additionally, the number of implants suffering from pathologic bone loss (>1.4mm) after 36 months was evaluated for both groups.

Results: The radiological peri-implant bone loss at the distal sites after 36 months was 0.72mm in the study group (median; 25-Q: 0.27mm; 75-Q: 1.11mm) and 0.37mm in the control group (25-Q: 0.15mm; 75-Q: 0.71mm). The difference between the groups is statistically significant ($p=0.004$).

At the mesial sites (study-group: 0.52mm; control-group: 0.41mm; $p=0.179$) and at all other examination intervals the differences between the two groups were not significant.

Neither did we find any statistically significant differences within the study-group between implants placed in the maxilla versus the mandible or in the anterior versus the posterior region.

The study group exhibited more implants suffering from pathologic bone loss (>1.4mm) than the control group (8 versus 4 implants).
**Biography**

- 1998-2003 Dentist student, University of Goettingen, Germany
- 2004-2015 Dental surgeon in private practice
- 2004-2015 training instructor for dental implantology and prosthodontics at the German Center of Implantology (DIZ, Detmold, Germany)
- since 2013 post-graduate doctoral student at the University of Witten/Herdecke, Germany (Dept. of Periodontology, doctorate supervisor: Prof. Dr. WD Grimm)
- lectures, book- and journal publications, hands-on training courses for the DIZ (German Center of Implantology)
Activation and migration of CD4+ lymphocytes induced by different “foreign bodies”

Abstract

Introduction: CD4+ play a crucial role in detection and destruction of foreign antigens as seen in the case of periodontitis or tumor immunology. However it is not clear whether and how metal alloys placed sub-gingivally or tumor cells could influence migration behaviour and activation status of CD4+. As previously reported we discovered that spontaneous migration of CD4+ cells is regulated by protein kinase (PTK) while induced migration is protein kinase C (PKC) dependent. Material and methods: In our study we compared the influence of two foreign pathogen groups (dental alloys and tumor cell lines) on CD4+ and recorded differences or similarities in activation status, migration behaviour and immune modulation of these cells. Methods: The locomotion of immunomagnetically isolated human blood lymphocytes was recorded by time lapse videomicroscopy using a 3-D collagen matrix and was analysed by computer assisted cell tracking. The activation status of CD4+ was assessed by a FACS analysis using CD25 and CD45R0. We tested two dental alloys (reduced precious rp, non-precious np), and their eluates. Results: While the mean percentage of CD4+ migrating was reduced by the two dental alloys compared to the controls (np 40%, rp 58%) the alloy eluates showed an increase in motility (np 85%, rp 36%). Direct contact of CD4+ with the alloys led to an upregulation of only CD45R0, while PBS-eluates of both alloys decreased the CD45R0 expression. Conclusion: Within the two groups of foreign bodies we observed opposite effects in migration and activation behaviour. At this stage of investigation we can not discriminate whether the effect recorded for the metal alloys is due to an extracellular or to an intracellular action. However, in either case we see that dental alloys impair the function of T lymphocytes. This model is suitable for further investigations of the signal transduction pathway and for the evaluation of modulating factors leading to an impaired immune response in immunologically compromised patients with periodontal disease.

Biography

1987–89 - the laboratory assistant, the senior laboratory assistant of the Student's Scientific Research Institute of occupational health and occupational diseases of StSMI.
1989 -- graduated StSMI with honours on speciality "General Medicine".
1989-95 - the assistant of the chair of Internal Diseases.
1995 – 2012 -- the assistant of the chair of Therapy of the faculty of postgraduate education.
1999- Ph.D, Therapy.
2012 -15 -- the director of the Center of scientific and innovative development of StSMU.
2015 – the head of the Center for personalized medicine of the Scientific and Innovative Association of StSMU.
The influence of porous titanium for the osteogenic potential of bone marrow cells in vitro and in vivo

Abstract
The experimental study involved 12 yearling sheep with a focus on the osteogenic potential of porous titanium used for subantral augmentation. The clinical study was performed on 33 patients aged 47–67, 10 females and 9 males, belonging to the study group (porous titanium used), and 14 patients of the control group aged 44–65 (6 males and 8 females) with calcium phosphate and bone collagen based materials used. The patients of the two groups had 46 and 32 implants installed, respectively. The experimental, the histological, and the clinical examinations showed that porous titanium granules are biologically compatible with bone tissue; they demonstrate optimal surface microrelief, which establishes conditions that facilitate adhesion and migration of the bone-forming cells. The granules also demonstrate insignificant resorption kinetics and ensure effective neovascularization in the newly developing bone tissue. Porous titanium can offer an effective alternative to calcium phosphate and bone collagen based materials used for subantral augmentation of the maxillary bone in cases of dental implantation and reconstructive and plastic maxillary sinus surgeries.

Biography
Сирак Сергей Владимирович, в 1996 году закончил стоматологический факультет СтГМА, обучался в клинической интернатуре, затем в клинической ординатуре. Докторскую диссертацию защитил в 2006 году в г. Москве в Центральном НИИ стоматологии и ЧЛХ. Возглавляет кафедру стоматологии с 2008 г. Автор 60 патентов РФ на изобретение и более 300 научных работ, опубликованных в системах цитирования РИНЦ, Web of Science и Scopus. Под научным руководством защищены кандидатские и докторские диссертации. Круг научных интересов — хирургическая стоматология, местное обезболивание, регенеративная медицина, клеточные технологии, инновационные разработки в области создания новых материалов и средств для стоматологии и челюстно-лицевой хирургии. Является обладателем ряда грантов на научную деятельность, полученных от различных фондов, научным руководителем нескольких победителей Федеральной программы СТАРТ и У. М. Н. И. К. (Фонда содействия развитию малых форм предприятий в научно-технической сфере при Правительстве РФ), обладателем гранта Бостонского университета (США).
Background and Overview
Since the early years of the 21st century it has been conducted studies and developed the clinical concept of 3D reconstruction of non-removable implant suprastructure in ceramic, at the same time raising the issue of the fast fabrication of the ceramic restorations. We are using in-office computer-aided design/computer-aided manufacturing (CAD/CAM) fabrication of ceramic restorations specifically to complete multiple ceramic restorations for implant patients. CEREC (Sirona Dental Systems GmbH, Bensheim, Germany) divided the system into an acquisition/design unit and a separate machining unit. Three-dimensional software makes the handling illustrative and easy both in the office and in the laboratory.

Clinical Implications
The process of planning and manufacturing of non-removable implant suprastructure in ceramics will be shown in the presentation.

Conclusions
Sound knowledge of diligent planning is essential for the successful integration of CAD/CAM into advanced implant dentistry. It appears that the CEREC CAD/CAM concept is becoming a significant part of regenerative dentistry.

Biography
Dental technician apprenticeship with degree 1987-1991
Studied dentistry at the Witten/Herdecke University 1995-2001, state examination, approval
Dental work: 2001-2005: Assistant Dentist, Department of Oral Surgery Faculty of Dentistry, Witten/Herdecke University
Since December 2005: own privat practice in Sprockhövel, practice team Hasslinghausen
Certified Practice Areas (Dental Association Westphalia-Lippe), since 2010:
• Aesthetic Dentistry
• Laser Dentistry
• implantology
15.15-15.30: Р. Донака, Аргон-групп, Германия
R. Donaca, chair, Argon Dental - part of Argon Group, Germany

Конические имплантологические системы поддерживают регенерацию альвеолярной кости

Conical implant systems support alveolar bone regenerative processes.

Abstract
The development of conical connections in dental implantology has been described in literature and scientific publications. In vitro studies indicated that conical abutments showed sufficient resistance to maximal bending forces and fatigue loading. Conical abutments showed superiority in terms of seal performance, microgap formation, torque maintenance, and abutment stability. In vivo studies (human and animal) indicated that conical and nonconical systems are comparable in terms of implant success and survival rates with less marginal bone loss around conical connection implants in most cases. Implant systems using a conical implant-abutment connection, provides better results in terms of abutment fit, stability, and seal performance. Through the special Morse taper construction of the Konus K3Pro implants from Argon Medical Productions GmbH & Co. KG of 3°; it is ensured a maximum seal between the implant and abutments. The Konus K3Pro implants ensures a micro-movement and micro-gap free connection.

Biography
ARGON Group. The Argon Group head office is located in Bingen am Rhein, Germany. Argon is an international manufacturer of complete dental implant systems designed for the basic, as well as the digital usage of today’s implantologist. The Argon Group is also a manufacturer/ distributor of allograft materials and accessories needed for basic, as well as advanced Hard- & Soft-Tissue reconstructions. All products from the Argon Group are designed, engineered and produced in Germany and carry the label “Made and Engineered in Germany”. Our products are distributed internationally and are sold solely to clinics, dentists, clinicians and labs for use in the field of implantology. Argon also offers and attends various national and international courses and congresses, where clinicians and labs can exchange or gain knowledge and information pertaining to the field of implantology.

Создание биологической матрицы органов и тканей грудной полости крыс и нечеловекообразных приматов

International Research, Clinical and Education Center of Regenerative Medicine, Kuban State Medical University, Krasnodar, Russian Federation

Biological scaffolds creation of rat’s and nonhuman primate intrathoracic organs and tissue

Abstract

Tissue engineering as a part of the regenerative medicine is an interdisciplinary field, applying the principles of cell transplantation, materials science and engineering to develop biological substitutes that establish or restore the physiological function. One of three tissue engineering’s main principles is the usage of a scaffold, i.e. a three-dimensional structure for cells to adhere to and grow on and can be either natural or artificially derived. The ideal biomaterial scaffolds for intrathoracic organs and tissue grafts should be non-toxic, resistance to infection, durable, elastic, biodegradable and support in vitro adhesion, growth and function of several cell types. In vivo acellular matrices should act as a template allowing the ingrowth of the host cells and can be remodeled in a living tissue. Biomaterials should not: provide an inflammatory reaction or rejection, allergy or sensitization, shrink in the healing process, be carcinogenic and initiate local complications. For biologically derived scaffold creation we used decellularization of donor organs. Decellularization uses physical or chemical means to eliminate immunogenic cells from the organ or tissue while preserving the native ultrastructure and composition of the extracellular matrix (ECM), which maintains the biomechanical properties of the organ. The optimal decellularization method varies depending on the tissue/organ. For intrathoracic organs and tissue (heart, lungs, diaphragm) decellularization on rats and nonhuman primates model were used detergent-enzymatic method (DEM). We applied the modified protocol with reduced detergent and enzymes exposure time and sequence: [Aqua MilliQ, Deoxycholate 4% (Sigma, Sweden), Triton-X 100 (Sigma, Sweden), PBS, DNase I, 2000 ku in 200ml PBS (Invitrogen, Sweden), EDTA, 800 um in 200 MilliQ (Sigma, Sweden)]. In decellularized organs were demonstrated that nuclei and other cell elements were absent. Moreover, the reciprocal orientation of fibers in scaffold walls resembled the control (native organ), and there were no signs of collagen and elastin degradation. Architectonics of intrafibrous connective tissue remained intact, preserved adventitia of small vessels. Nuclei structures fluoresced intensively in native organs, in decellularized organs there was no fluorescence. In vitro studies have revealed that 24 hours were necessary for the complete removal of the cellular part of the tissue, including the disappearance of the specific tissue protein as tropomyosin and the MHC class I, MHC class II, von Willebrand factor. We have determined that these protocols have minimum negative effects on extracellular matrix composition, ultrastructure and biocompatibility
properties. Our suggestion confirmed by undamaged histo-architecture and ultrastructure (SEM) of extracellular matrix without fragmentation and loss its structure. Moreover, we observed the presence of extracellular proteins such as collagen I, collagen IV, laminin, fibronectin, elastin. Lack of immunogenicity was also confirmed by DNA quantification of the decellularized matrices. Moreover, decellularized matrices preserved important biomechanical properties. Measured mechanical properties demonstrate, that both native and decellularized organs possess almost same properties in this test. Our data obtained in vitro from MTT assay, Live/Dead assay suggested that the seeded graft contained attached cells that were viable and proliferating on surfaces. It could be demonstrate that the matrix degradation products did not exert any toxic effect on cell viability.

In conclusion, we believe that these protocols of obtainment heart, lungs, diaphragm matrices which was structurally and mechanically similar to native organs opens the door to the creation of clinically functional, fully tissue-engineered intrathoracic organs and tissue replacements in the near future.

Acknowledgments:
This work was supported by Bioengineering of Tracheal Tissue and the Government of the Russian Federation Grant (Agreement No. 11.G34.31.0065).
Мастер-класс
по продвинутой имплантологии с
применением алlogenной кости при
непосредственной (immediat implant
placement) имплантов

Master class
on advanced implantology

Organized and presented by Stavropol State Medical University,
Department of Stomatology (Chair: Prof. Dr. S.V. Sirak), Russian
Federation

as part of II. International Symposion
«Age of Regenerative Medicine»

15.05.2015 10:00-16:00

Место проведения: СтГМУ, ул. Мира, 310. Методический кабинет.
Стоматологическая клиника «Аполония», Ставрополь, ул. Пирогова 30а.
Location: Department of Stomatology (Chair: Prof. Dr. S.V. Sirak), Apolonija,
Stomatological Clinic, Stavropol, Pirogova str., 30a

Содержание теоретического курса
The content of the theoretical course
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Master-class «Advanced implantology»

Место проведения – клиника «Аполоний», Ставрополь, Россия.
Department of Stomatology (Chair: Prof. Dr. S.V. Sirak), Stomatological Clinic «Apolinariya», Stavropol, Pirogova str., 30a

Профессор Б.Гиссенхаген, Университет Франкфурт на Майне, Германия, Центр Имплантологии Касселя, Германия, Профессор В.Д. Гримм, СтГМУ, Ставрополь, Россия, Виттен/Хердека Университет, Германия, Prof. B. Gissenhagen, prof W.-D. Grimm

Лекторы и преподаватели мастер-классов
Lecturers and presenters, Life Surgical Procedures

Dr. Б. Гиссенхаген, Франкфуртский Университет, Центр имплантологии Касселя, Германия
Dr. B. Giesenhagen, University of Frankfurt/M., Germany, Implant Center Kassel, Germany

1980-2011 -Dental Practice in Melsungen.
1996 - Medical Director PRO-IMPLANT, Institute for Implantology and Education.

- Academic Association with Johann Wolfgang Goethe University Frankfurt/Main
- Since many years involved in different educatione programs in Germany and abroad.
- Developer of the Bone Ring Technique.
- Well known specialist for augmentation of hard and soft tissue around the world
- Numerous publications about augmentation and Bone Ring Technique.

2012 - Privat Clinic for Implantology in Kassel, Germany
Wolf-Dieter Grimm, DDS, PhD, MSc, Professor of Periodontology
Professor of Stomatology, Department of Stomatology, Stavropol State Medical University, Visiting Professor of Periodontology, Gottfried-Herder-Program, German Academic Exchange Services (DAAD)
Periodontology, Department of Dental Medicine, Faculty of Health, University of Witten/Herdecke, Germany

Specialty Certification
1. Diplomate, Periodontology, German Federation of Periodontology (DGP) and European Federation of Periodontology (EFP)

Academic Degrees and current positions
- Dr. med. dent., University of Dresden, Medical Academy, Dental School,
- Dr. sc. med. (PhD), University of Dresden, Medical Academy, Dental School, Department of Periodontology
- Dr. med. dent. habil. (PhD), University of Witten, School of Dental Medicine, Department of Periodontology
- Adjunct Professor of Periodontology: University of North Carolina at Chapel Hill, Department of Periodontology, 1997-2005
- Professor, University of Witten, Department of Dental Medicine, Department of Periodontology, Faculty of Health, 1991-
- Privat Practice, Team Hasslinghausen, 2010-
- Visiting Gottfried Herder Program Professor, Stomatology, Stavropol State Medical University, Russian Federation, 2014-

Research Fields
- Epidemiology and Etiopathogenesis of Periodontal Diseases, Large Scale Investigations
- Periodontal Disease and Systemic (Genetic) Diseases, Diabetes Mellitus, Down Syndrome
- Microbial Colonization of human and „artificial“ Tooth Surfaces, 3D Cell Migration and Gene Micro Arrays
- Guided Tissue Regeneration and Periodontal Microsurgery
- Guided Bone Regeneration and Periodontal Microsurgery
- Dental Care for Handicapped
- Image processing for functional analysis (NMR, CT, DVT)
- Adult stem cell research in periodontal tissue regeneration
17 articles in Textbooks, Editor of Textbook, 128 Publications in peer-reviewed national and international Journals, 2x Member of Journal Boards, 2x Winner of Awards from Dental Societies.

Мастер-класс «Передовые клеточные технологии»

Master-class «Advanced steam-cell technology»

Зал «Звездочка»

Hall «Star» Lecturers and presenter

Prof. Dr. D. Widera, Lecturer in Stem Cell Biology and Regenerative Medicine, Head of the Stem Cell Biology and Regenerative Medicine Group, Reading School of Pharmacy, University of Reading, United Kingdom

Neural Crest-Derived Stem Cells as a Tool in Regenerative Dentistry

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Keywords: neural crest-derived stem cells, regenerative dentistry, regeneration
Conflict of Interest Disclosure: The author declares no conflicts of interest

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Stavropol, Russian Federation
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Abstract
The embryonic neural crest appears during development of mammals including humans as a transient structure between the newly formed ectoderm and the neural tube. Due to their intrinsic ability to give to mesenchymal and ectodermal derivatives neural crest stem cells possess an extraordinarily high developmental potential surpassed only by totipotent cells of the zygote and pluripotent embryonic stem cells. Adult neural crest-derived stem cells (NCSCs) were long term believed to be an in vitro phenomenon similar to embryonic stem cells derived from the inner cell mass of a blastocyst. During the last 15 years, however, an emerging line of evidence supported the hypothesis that at least a limited number of adult NCSCs may exist in the human body even in the adulthood. Remarkably, such adult NCSCs perform self-renewal and exhibit a differentiation potential comparable to their embryonic counterparts. In particular they can give rise to neurons, melanocytes, bone cells and cartilage in addition to many cells types associated with tooth development and homeostasis.

In the following I briefly review the current knowledge on the sources of human NCSCs within the oral cavity, discuss their potential in the regenerative dentistry and present relevant research of my lab.

1. Regenerative dentistry
Regenerative dentistry is a branch of translational stem cell biology focusing on replacing and regenerating dental tissues to restore or re-establish their normal function lost during degenerative diseases or acute lesions. The regeneration itself can be achieved through transplantation of autologous or allogenic stem cells, or by improving the tissue self-repair mechanisms (e.g. by application of growth factors). In addition, a combination of stem cells and bone implants can be used to improve the tissue integration and the clinical outcome. As the oral cavity represents a complex system consisting of teeth, bone, soft tissues and sensory nerves, the regenerative dentistry is a challenging and emerging field within regenerative medicine.

2. Neural Crest-Derived Stem Cells
The neural crest was first described as the 'Zwischenstrang' (German, 'zwischen': between; 'Strang': cord) by the Swiss anatomist and cardiologist Wilhelm His. His described the neural crest as a transient embryonic structure arising at the fusion line between the invagination of the neural tube and the epidermis during chicken embryo development. Such neural crest cells migrate out of their niche soon after neurulation took place and engender various populations of cells in the adult body including peripheral neurons, melanocytes, Schwann cells but also mesenchymal cells types including cranial bones, cartilage and fat cells. Remarkably, defects of neural crest are associated with severe malformations of the human heads including cleft lip and cleft palate. Neural crest cells are the embryonic origin of most dental cell types and surrounding tissues including odontoblasts, cementoblasts in addition to the dental pulp, the periodontium and the alveolar bone \(^1\). This developmental origin of
the tooth has been spectacularly demonstrated by Mitsiadis in 2003. In this study, xenogenic transplantation of mouse neural crest into a chicken embryo resulted in development of tooth-like structures. Remarkably, adult human neural crest-derived stem cells (NCSCs) can be found in different tissues and organs, especially within the craniofacial region. Such adult human NCSCs are able to undergo self-renewal and possess a surprisingly high differentiation potential in vitro and in vivo (reviewed in). Importantly, NCSCs can be isolated from the given patient and transplanted as an autograft. Due to their easy accessibility and the intrinsic ability to give rise not only to dental cells and structures but also in neurons and bone cells, NCSCs represent an ideal stem cell type for the use in regenerative dentistry. Concerning the marker expression most adult human NCSC populations are characterised by the expression of the intermediate filament Nestin, the surface receptor p75NTR (CD271) and the carbohydrate HNK-1 in addition to the neural crest specific transcription factors Snail and Twist in vitro and in vivo (see for a full marker list).

3. Sources of NCSCs within the Human Oral Cavity
Human NCSCs can be readily isolated from a variety of adult tissue (see Figure 1). One prominent example for human NCSCs are the so called olfactory ensheathing cells (OECs). Besides the fact that OECs are very plastic and represent a promising NCSC source, the potential use of this NCSC-source suffers from fact that the total area of olfactory epithelium represents 3% of the total surface area of the nasal cavity and gets gradually replaced by respiratory epithelium during aging. However, also the respiratory epithelium harbours a cell population with a high regenerative potential. This has been suggested by a study demonstrating that transplantation of human inferior turbinate tissue is sufficient for an efficient closure of small and medium-sized nasal septal perforations. Such regenerative capacity can be explained by the presence of a distinct NCSC population in the human respiratory mucosa. In our lab, we indeed identified a new NCSC type residing in the lamina propria underlying the respiratory epithelium. The secondary palate represents a further highly regenerative tissue within the human craniofacial compartment, which develops under direct contribution of neural crest cells. Notably, even medium sized wounds within the palatal mucosa heal rapidly. This capability for rapid regeneration can be explained by the presence of NCSCs within the palatal mucosa. Such palatal NCSCs can be found in rodent as well as in human palate and express several neural crest-specific markers including p75, Nestin, and Snail. A further NCSC population can be readily isolated from the buccal mucosa lamina propria. Such NCSCs from the human oral mucosa express Snail, Slug, Sox10 in addition to Twist.
Another lab identified a source of p75 expressing NCSCs within the human gingival and alveolar mucosa. In 2007 we were able to cultivate periodontal NCSCs under serum-free conditions leading to formation of neural crest-like neurospheres able to give rise to neuronal and bone cells. In accordance with our results, Huang and colleagues demonstrated that human periodontal NCSCs isolated from impacted wisdom teeth of young adults express Nestin, Slug, p75 and Sox10 and can give rise to neuronal and osteogenic lineages.

4. Isolation and Cultivation of human NCSCs

Human NCSCs can be easily isolated and enriched based on the expression of the receptor p75 (CD271). After mechanical and enzymatic dissociation of the tissue (using e.g. Dispase and Collagenase) p75-expressing cells can be labelled with an antibody raised against the extracellular domain of the receptor followed by separation using flow cytometry (FACS) of magnetic cell separation (MACS) which is available even in clinical scale (Miltenyi Biotec, CliniMACS® System). Theoretically, separated NCSCs could be directly re-transplanted back into the patient. However, the relative abundances of available endogenous NCSCs in their niches within the human body are too low to achieve significant therapeutic effects if re-transplanted without prior ex vivo expansion. Thus, efficient cultivation protocols are required prior to clinical use of NCSCs. Routinely, adult human stem cells are cultivated in a medium comprising foetal calf serum (FCS). FCS provides important supplements such as growth factors and assures optimal growth and cellular viability. However, there are several cautionary notes concerning the transplantation of human stem cells cultivated with FCS. Due to its bovine origin, there is a residual risk of transmitting infectious agents such as animal-borne pathogens. Moreover, transplantation of autologous cells exposed to FCS can cause immune response reactions in the human body. Therefore animal serum-free cultivation approaches have been developed including cultivation of NCSCs in presence of the growth factors FGF-2 and EGF leading to efficient neurosphere formation (see Figure 2).
Figure 2. Cultivated human palatal NCSCs cells form self-adherent neurospheres and express the intermediate filament Nestin. Human palatal NCSCs were isolated according to protocol described in 6, fixed using 4% paraformaldehyde and stained using primary antibody against human Nestin and Alexa 555-coupled secondary antibody. DNA was stained using SYTOX green (bar 20 μm). Figure and figure legend from 24. Copyright © 2012 Darius Widera et al.

Although very promising, the lack of optimal support with growth factor in serum-free medium often reduces the proliferation capability of adult stem cells, making their use in clinical praxis problematic 25. In this respect it is noteworthy that according to a recommendation of the Food and Drug Administration (FDA), the cultivation time of human stem cells for transplantation purposes should not exceed five weeks to avoid the risk of culture induced tumorigenic transformation 26. In our lab, we developed a new cultivation method for NCSC based therapeutics based on the used of human blood plasma 27 (see Figure 3).

Figure 3. Cultivation of human NCSCs within human blood plasma-derived matrix. Human NCSCs were transiently transfected with GFP and cultivated as neurospheres. After dissociation of the spheres (top left) NCSCs were expanded as 3D culture embedded in the matrix (top right) not only on the top or at
the bottom of the matrix as visualised using confocal laser scanning microscopy. Figure taken from the OA version of 27. Copyright © 2011 Greiner et al.

In this approach we showed that adult human neural crest-derived stem cells can be grown in a 3D blood plasma matrix resulting in increased proliferation, unchanged ploidy and capability for self-renewal as well as remaining potential to differentiate into neuronal and osteogenic lineage. Our findings emphasise the potential of this cultivation method for cultivation of NCSCs for their application in complex regenerative approaches, like the treatment of craniofacial defects or within regenerative dentistry. Since NCSCs and human blood plasma can be theoretically obtained from the same patient, this approach is personalisable and potentially reduces the exposure of of the graft to xenogenic ingredients to a minimum. In a further approach we combined the cultivation of human NCSCs with a closed, clinical GMP-graded Afc-FEP bag system (see Figure 4.)

Figure 4. Human NCSCs grow three-dimensionally in clinical grade culture bags. (A) Afc-FEP bag containing NCSCs in medium supplemented with human blood plasma. (B) Phase contrast microscopy image of bag-cultured NCSCs revealing characteristic morphology comprising long-shaped cell bodies. (C) Confocal laser scanning microscopy analyses (Z-sectioning) followed by three-dimensional-reconstruction showed three-dimensional-growth of bag-cultured NCSCs previously transfected with GFP. Figure taken from the OA version of 28. Copyright © 2014 Greiner et al.

5. Summary
- Human craniofacial tissue contains NCSC, which can be readily isolated
- NCSCs can give rise into, neuronal, mesenchymal and dental cell types
- Adult human NCSCs can be expanded in a serum-free, closed and clinically approved cell culture system
NCSCs are ideal candidates for the future use in regenerative dentistry

6. Acknowledgment
DW is supported by a grant of the German Research Foundation DFG (Grant WI4318/2-1) and start-up funds of the University of Reading, UK. The figures 2, 3 and 4 are taken from open access versions of articles from our lab.

7. References
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**About us**

We are an academic research laboratory at the School of Pharmacy, University of Reading, (Berkshire, United Kingdom) interested in adult stem cell research as well as in the influence of injury and inflammation on somatic cells (injury-induced cellular reprogramming). We want to understand, how inflammatory signalling pathways influence (de-) differentiation, proliferation and migration of different (stem) cell types.

![Reading School of Pharmacy, Whiteknights Campus, University of Reading](image)

In addition, we work on novel human and murine neural crest-derived stem cell populations, which are promising candidates for the development of autologous, cell-based therapies in the context of regenerative medicine.

We further apply advanced, modern approaches to address stimulus-dependent behavior of receptors (especially tumor necrosis receptor I and Toll-like receptor 4) and the resulting downstream signalling in stem cells and cancer (tumour) stem cells.

We are actively searching for industrial partners to commercialise our research and ideas.

**Web:** [http://www.wideralab.org](http://www.wideralab.org)

**Biography**

**h-Factor:** 12 (ISI Thompson), 15 (Google Scholar)

**citations:** 645 (ISI Thompson, 17.10.2014), 972 (Google Scholar, 17.10.2014)
original research papers: 33 (14 as first/senior author)
reviews: 6 (5 as first/senior author)
book chapters: 3
ResearcherID: J-4237-2012
ORCID: 0000-0003-1686-130X
Google Scholar: http://scholar.google.de/citations?user=xPxpC2kAAAAJ

Education and Training
11.2012 Habilitation (German professorial qualification) and “venia legendi” for Cell Biology at the University of Bielefeld, Faculty of Biology, Germany
Habilitation-Thesis: “Alternative sources of adult stem cells for neuronal regeneration and the role of NF-κB in endogenous neural stem cells and neurons”
07.2007 Dr. rer. nat. (PhD) in Neurobiochemistry at the Institute for Neurobiochemistry (Kaltschmidt Lab), Witten/Herdecke University, Germany.
Grade: summa cum laude (with distinction)
11.2004 Diploma in Biochemistry (Dipl. Biochem.) at the Witten/Herdecke University, Germany. Grade: 1,0 (A)
Diploma Thesis at the Institute for Neurobiochemistry: “MCP-1 induces migration of adult neural stem cells”
10.2002 Intermediate diploma in Biology at the University Cologne, Germany

Positions and Employment
03.2013-present Project Leader / Senior Research Associate (Privatdozent), University of Bielefeld, Bielefeld, Germany, Department of Cell Biology
Main research topics: TLR4-mediated signaling in neural stem cells, cellular de-differentiation/reprogramming of Schwann cells; isolation, characterization, differentiation and transplantation of adult human and murine neural and neural crest-derived stem cells in animal models, development of novel high- / super-resolution microscopy methods for biological applications
10.2007-03.2013 Research Associate (Postdoc), University of Bielefeld, Bielefeld, Germany, Department of Cell Biology (Kaltschmidt Lab)
Main research topics: isolation and characterization of
adult neural and human neural crest-derived stem cells (periodontium, hard and soft palate, respiratory mucosa); the role of NF-kB in the nervous system, cellular reprogramming

12.2006-10.2007 Research Scientist (Postdoc), Molthera GmbH, Witten, Germany, Research & Development
Main research area: adult periodontal neural crest-derived stem cells; microarray analysis of oral and periodontal microflora in patient samples

2004-2007 Graduate Student, Witten/Herdecke University, Germany, Institute for Neurobiochemistry (Kaltschmidt Lab)
Research focus: human periodontal stem cells, the role of NF-kB in adult neural stem cells, application of human periodontal stem cells in critical size defect rat model of complex regeneration

2002-2004 Working student, Miltenyi Biotec, Research & Development (Assenmacher Lab, Hupert Lab, Piechaczek Lab), Bergisch Gladbach, Germany,
main research area: isolation and trans-differentiation of adult hematopoietic stem cells, software validation for the CliniMACS system

Honors, Grants and Awards

2014 Grant of the DFG (German Research Foundation) for the project “Mechanisms of neural TLR4-signaling”

2013 Selected by the Alexander von Humboldt Foundation (as one of five outstanding German stem cell scientists) as participant to the 7th Sino-German Frontiers of Science Symposium (section Stem Cells and Reprogramming) in Kunming, China, 20-23.03.2014

2013 Participation to the Gordon Research Conference “Neural Crest and Placodes” (invited), 21.07-26.07.2013, Easton, MA, USA

2013 Grant of the University of Bielefeld (FiF/Förderung Innovativer Forschung) for the project: "Investigation of the ligand-induced oligomerization of TLR4 in neural stem cells and neural cell lines"

2011 Grant of the University of Bielefeld (FiF/Förderung Innovativer Forschung) for the project: "The role of Schwann cells as novel, multipotent neural crest-derived stem cell population"
2009
Grant of the University of Bielefeld (FiF/Förderung Innovativer Forschung) for the project: "adult neural crest-derived stem cells"

2007
Award of the Rotary Foundation for the contribution to stem cell research

2006
Grant of the Besthorn Foundation for the project "mathematical modeling of neural stem cell proliferation"

2005
Travel grant of the Stem Cell Spring School Regenerative Medicine, University of Rostock

**Invited Talks at International Conferences**

1. *Highly efficient neuronal differentiation of human inferior turbinate stem cells*
   Meeting of the GMB study group “Molecular Neurobiology”
   September 15, 2012, Bochum, Germany

2. *Isolation and cultivation of human neural crest-derived stem cells for cell-based therapies*
   Biotechnica, Life Science Spotlight, October 12th, 2011, Hannover, Germany

3. *The role of NF-kB in adult neural and neural crest stem cells*
   3rd Molecular Cell Dynamics Meeting, May 6th, 2009, Münster, Germany

4. *Human periodontium-derived neural crest stem cells: chance or risk?*
   4th International Meeting of the Stem Cell Network North Rhine Westphalia
   October 9, 2007, Düsseldorf, Germany

5. *Inflammation and adult neural stem cells*
   Stem Cell Spring Meeting, University of Rostock
   June 3, 2005, Rostock, Germany

**Skills and Techniques**

**Management skills**
- Planning and coordination of research projects including supervision of BSc-, MSc-, PhD-students and technicians, publication of data in international, peer-reviewed journals
- Writing of progress reports, scientific papers (original research papers, reviews and book chapters), grant and patent applications
- Independent responsibility for the budget and individual administrative competence

**Laboratory techniques**
- Routine laboratory techniques (PCR, RT-PCR, qPCR, WB, molecular cloning, ICC, IHC etc.)
- Primary cell culture (organotypic hippocampal cultures, MSCs, neurons, glial cells, Schwann cells)
- Isolation, cultivation, characterization and differentiation of adult stem cells (hematopoietic stem cells, neural stem cells, adult human and rodent neural crest-derived stem cells)
- 3D cell culture (incl. method development)
- Confocal microscopy (incl. advanced techniques e.g. sub-diffraction triexciton imaging, FRAP, live cell imaging)
- Reprogramming to multipotency (Schwann cells into neural crest stem cells) and pluripotency (iPS)
- Flow cytometry (including sorting and development of methods)

Teaching
- Independent teaching in English and German (general Cell Biology, Biochemistry, Stem Cell Biology and Regenerative Medicine) including practical courses and lectures for B.Sc., M.Sc. and PhD-student at University of Witten/Herdecke, University Bielefeld, and annual lecture series “Biochemistry of Stem Cells” at the Ruhr-University Bochum, Germany

Languages
- German: native
- Polish: native
- English: fluent

Computer skills
- Win, OS (Mac), Office (PP, Word and Excel), SAP, Graphics (Adobe, Corel, ImageJ), FlowJo, CellQuest, Zeiss Zen etc.

Professional Activities and Memberships
- Member of the German Stem Cell Network (GSCN)
- Member of the executive steering committee of the Light Microscopy Technology Platform, University of Bielefeld (LiMiTec, http://web.biologie.uni-bielefeld.de/imaging)
- Member of the Stem Cell Network North Rhine Westphalia
- State-approved project leader according to German Genetic Engineering Act (§15 GenTSV)
- ad-hoc referee for the German Academic Exchange Service (DAAD), Neurological Foundation Of New Zealand, the "Jubiläumsfonds der Österreichischen Nationalbank zur Förderung der Grundlagenforschung in Österreich" (Foundation of the Austrian National Bank for Basic Science), University of Luxemburg and for the journals FEBS letters, Stem Cells and Development, Stroke, Cell Biology International, Molecular and Cellular Endocrinology, Stem Cell Research and Therapy, Neuropharmacology, Clinical and Developmental Immunology, Langmuir
• Associate Editor (Biology) at Versita Publishing (De Gruyter group) (2012 - 2013)

Collaborations

Academic collaborations

Prof. Mike Heilemann, Institut für Physikalische und Theoretische Chemie, Goethe-Universität Frankfurt am Main, Germany
- Joined DFG (German Research Foundation) founded project (Topic: „Investigation of TLR4 oligomerization in neural cell lines and neural stem cells“), super-resolution imaging of the Tumor Necrosis Factor receptor I and Toll-like receptor 4 (dSTORM, uPAINT).

Prof. Dr. Wolf-Dieter Grimm, Department of Periodontology, Witten/Herdecke University
- Isolation, characterization and application of adult human periodontal and palatal stem cells in regenerative medicine Prof. Dr. Robert Sader, Mund-, Kiefer-, Plastische Gesichtschirurgie, Universitätsklinikum Frankfurt
- Isolation of neonatal and adult human stem cells from hard palate tissue

Prof. Dr. Thomas Dittmar, Witten/Herdecke University, Witten, Germany
- Analysis of migratory behavior of neural stem cells and glioblastoma cells after pro-inflammatory stimuli

Prof Dr. Hermann Rohrer, Max-Planck-Institute for Brain Research, Research Group Developmental Neurobiology, Frankfurt/M, Germany
- Reprogramming of neural crest-derived peripheral nervous system progenitors into central nervous system phenotype

Prof. Holger Sudhoff, Klinikum Bielefeld; Hals-, Nasen-, Ohrenheilkunde, Kopf- und Halschirurgie, Bielefeld, Germany
- Investigation of the cellular origin of Acusticus Neurinoma, Isolation and characterization of adult stem cells from the adult human inferior turbinate

Dr. Margriet Huismann, LUMC. Universiteit Leiden, Netherlands
- Development of novel method for isolation of highly purified epidermal neural crest stem cells (EPI-NCSCs)

Dr. Anje Sporbert, Max-Delbrück-Centrum for Molecular Medicine, 2-Photon and Confocal Microscopy Core Facility, Berlin, Germany
- High resolution Tri-Exciton-confocal-imaging of biological probes

Dr. Jean-Baptiste Sibarita, IINS, Bordeaux, France
- Super-resolution live cell imaging (sptPALM) of the transcription factor NF-kappaB and the Tumor Necrosis Factor Receptor I

Industry cooperations

Serva Electrophoresis/Normark Pharma, Germany
- Development of protocols for inactivation of collagenase after isolation of adult human neural crest stem cells

Miltenyi Biotec GmbH, Bergisch Gladbach, Germany

- Optimization of stem cell isolation based on expression of PSA using MACS technology (finished)
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