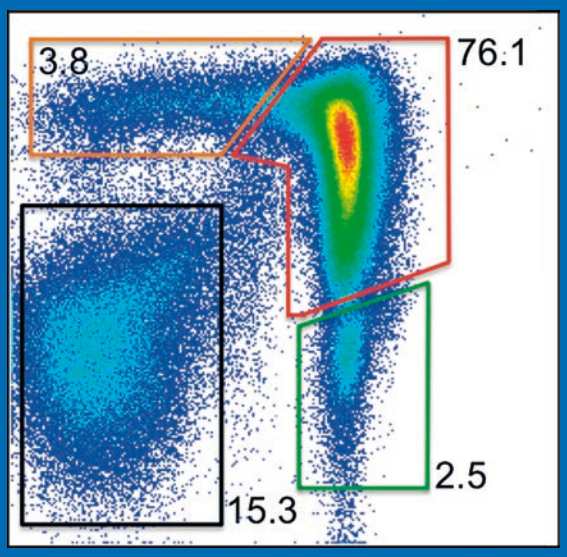
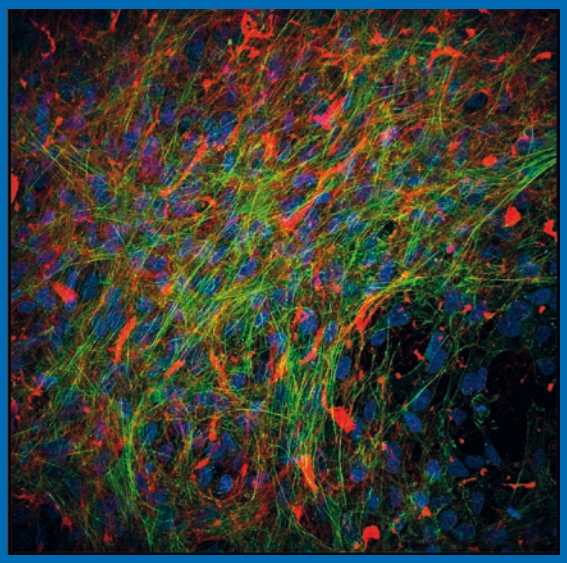
Gene Function in Cell Growth, Differentiation & Development





Director

Univ.-Prof. Dr. rer. nat. Martin Zenke

Institute for Biomedical Engineering – Cell Biology
RWTH Aachen University Hospital
Pauwelsstrasse 30, 52074 Aachen

Helmholtz Institute for Biomedical Engineering
Pauwelsstrasse 20, 52074 Aachen

Phone: +49-241-80 80760 (Office)
+49-241-80 80759 (Secretary)
Fax: +49-241-80 82008
Email: martin.zenke@rwth-aachen.de
Web: http://www.molcell.de
http://www.stemcellfactory.de

Staff

Mierau, Eveline, Administrative Assistant

Aydin, Gülcan, BSc, Technician
Böhnke, Janik, MSc, PhD student
Dassen, Yannick, MSc Student
Götz, Katrin, MSc, Technician
Hamouda, Ahmed, MSc, PhD Student
Hapala Jan, PhD, Postdoc
Hieronymus, Thomas, PhD, Group Leader
Look, Thomas, MSc Student
Ludwig, Carsten, MSc Student
Ma, Zhiyao, MSc Student
Prithivirat, Sujeethkumar, MSc Student
Riegert, Janine, MSc Student
Schalla, Carmen, Technician
Schurse, Henning, MSc Student
Sebastian, Raja, PhD, Visiting Scientist
Sechi, Antonio, PhD, Group Leader
Seré, Kristin, PhD, Group Leader
Szymanski de Toledo, Marcelo, PhD, Postdoc
Wanek, Paul, BSc, Technician

Stem Cell Biology and Cellular Engineering

Univ.-Prof. Dr. med., Dr. rer. nat. Wolfgang Wagner

Helmholtz Institute for Biomedical Engineering
Pauwelsstrasse 20, 52074 Aachen

Phone: +49-241-80 88611 (Office)
Fax: +49-241-80 82008
Email: wwagner@ukaachen.de
Web: http://www.stemcellbiology.ukaachen.de

Božić, Tanja, MSc, PhD Student
Bocova, Ledio, MSc, PhD Student
Brecht, Johanna, MSc Student
Cypris, Olivia, MSc, PhD Student
Eipel, Monika, MSc, PhD Student
Fernandez-Rebollo., Eduardo, PhD, Postdoc
Franzen, Julia, MSc, PhD Student
Frobel, Joana, MSc, PhD Student
Göbel, Carolin, MSc Student
Goetzke, Roman, MSc, PhD Student
Grezella, Clara, MSc Student
Hapala, Jan, PhD, Postdoc
Han, Yang, MSc, PhD Student
Hollmann, Jonathan, MD Student
Lubberich, Richard, MD Student
Nüchtern, Selina, BSc, Technician
Ostrowska, Alina, BSc, Technician
Schmidt, Marco, MSc, PhD Student
Tharmapalan, Vithurithra, MSc Student

Introduction

The scientific progress made in recent years with both adult and pluripotent stem cells demonstrates the importance of stem cell research and its impact on biology and biomedicine. Additionally, engineering of stem cells possesses enormous potential for tailoring biomedical applications and cellular therapies towards precise and personalized medicine. This also demonstrates that engineering principles enter biology and biomedicine.

The institute studies genetic programs and epigenetic mechanisms that determine cell identity and developmental potential of stem cells and their differentiated progeny. A particular focus is on hematopoietic stem cells (HSC), mesenchymal stem cells (MSC), and embryonic stem cells (ES cells) and on stem cell differentiation towards specific lineages, such as antigen presenting dendritic cells (DC). In addition, pluripotent stem cells are generated from somatic cells by reprogramming, referred to as induced pluripotent stem cells (iPS cells; Fig. 1).

Novel technologies of genome editing including CRISPR/Cas have revolutionized both basic and applied research in many areas of biology and biomedicine. Stem cells are particularly well suited for genome editing. Thus, one objective of our research is on stem cell engineering and the generation of cells with wanted properties e.g. for disease modeling or drug testing.

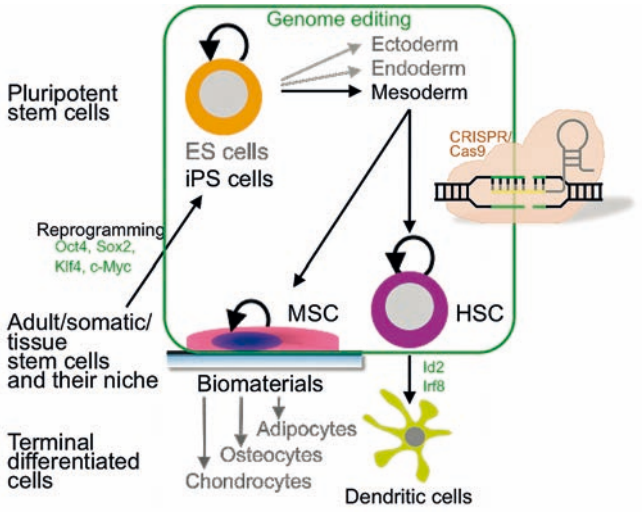


Fig. 1: Cellular and genetic engineering identifies genetic programs of cell fate. Transcription factors (green) are investigated and used to influence developmental programs. Mesenchymal stem cells (MSC) and hematopoietic stem cells (HSC) reside in the bone marrow niche and develop into cells of connective tissue and all cells in blood, such as dendritic cells, respectively. Biomaterials are used to emulate aspects of the niche and impact on cell growth, differentiation, and function. Induced pluripotent stem cells (iPS cells) are obtained from somatic cells by reprogramming. CRISPR/Cas technology is employed for precision genome editing of stem cells.

Stem cells and their differentiated progeny develop in a highly specialized microenvironment, referred to as stem cell niche. Thus, a further objective of our research is to employ biomaterials and/or specific factors to recapitulate conditions of the stem cell niche in vitro for optimal growth and differentiation of stem/progenitor cells. A particular focus is on DC development and DC migration. This includes research on molecular mechanisms of cell-to-cell and cell-biomaterial interaction and their impact on cell motility and adhesion. Furthermore, mechanisms of genetic and epigenetic regulation are investigated to address their impact on cellular senescence and aging of stem cells and on DC development. These studies are expected to provide valuable insights for cell and tissue engineering that may lead to novel replacement therapies in regenerative medicine.

Induced Pluripotent Stem Cells and Precision Genome Engineering

Patient specific iPS cells represent an essentially inexhaustible cell source for many biomedical applications. Additionally, iPS cells are ideally suited for genome editing with CRISPR/Cas, since the genetic changes introduced are propagated to the daughter generations, including differentiated cells (Zenke et al., 2018). We use patient and disease specific iPS cells and genome editing with CRISPR/Cas for studies on the impact of mutated KIT, JAK2 and calreticulin in leukemia and for compound screening (in collaboration with Department of Hematology, Oncology, Hemostaseology and Stem Cell Transplantation, RWTH Aachen University Hospital, and Organic Chemistry, RWTH Aachen University, and Department of Medicine I and Ludwig Boltzmann Cluster Oncology, Medical University, Vienna, Austria). In addition, iPS cells of patients with chronic pain were generated to study the pathophysiology of pain (Meents et al., 2018; in collaboration with Institute of Physiology, RWTH Aachen University Hospital).

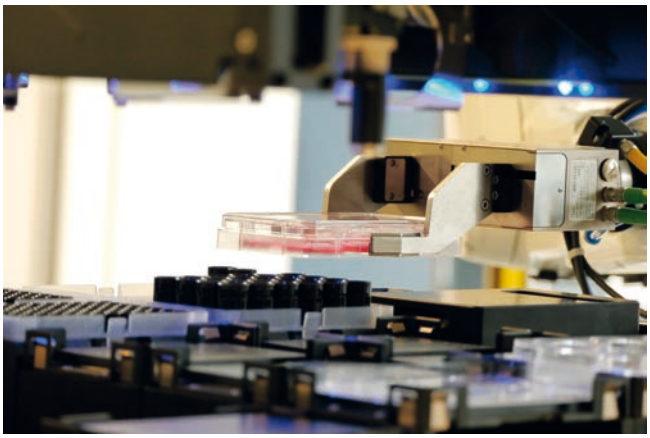


Fig. 2: Automatic cell production facility (iCellFactory)

Biomedical applications of iPS cells, and of cells derived thereof, require processing of large numbers of individual cell products. To meet these needs we followed up on our efforts to construct an automatic cell production facility (Fig. 2; in collaboration with Laboratory for Machine Tools and Production Engineering, WZL, RWTH Aachen University and Fraunhofer Institute for Production Technology, IPT, Aachen, Germany; Malik et al., 2018).

Chromatin Architecture of Dendritic Cells

DC are professional antigen presenting cells that develop from HSC in bone marrow through successive step of lineage commitment and differentiation. In our previous work by Lin et al. (Nucleic Acids Res., 2015) we studied gene expression in DC and several histone modifications. We have now extended this work to map the genome-wide open chromatin architecture by transposase-accessible chromatin using sequencing (ATAC-seq) technology (Fig. 3 and Li et al., 2018). Chromatin architecture, transcription factor binding and histone modifications are being integrated by bioinformatics to device the transcriptional circuitry of DC development and function.

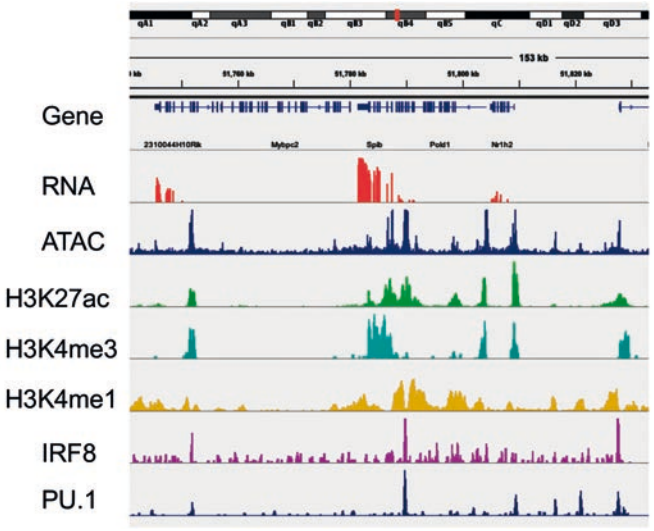


Fig. 3: SpiB locus in plasmacytoid DC subset was analyzed for gene expression (RNA), open chromatin (ATAC), histone modifications (H3K4me1, H3K4me3 and H3K27ac) and transcription factor binding (IRF8 and PU.1).

Cytokine Signals as Relays in Genetic Programs of EMT and MET during Dendritic Cell Development

DC develop from HSC in bone marrow (Fig. 1) and migrate as precursors into peripheral tissues, such as skin (Fig. 4). There, DC are embedded sedentarily and functionally to act as guardians of the immune system. Following antigen uptake, DC are activated, leave the peripheral tissue and migrate via lymphatic vessels to lymphoid organs for T cell stimulation (Fig. 4). We propose the concept that genetic programs of mesenchymal-to-epithelial transition (MET) and epithelial-to-mesenchymal transition (EMT) regulate homing and migration of DC, respectively (Hieronymus et al., Semin. Cell Dev. Biol., 2015; Sagi and Hieronymus, 2018). In EMT and MET programs distinct cytokine signals act as relays during DC development, function and migration. We particularly focus on investigating signaling via TGF-β receptor and hepatocyte growth factor (HGF) receptor, which have a differential impact on regulating homing and migration of DC (Fig. 4). The differential and sequential role of BMP7 and TGF-β1 in differentiation of Langerhans cells, the contingent of DC in stratified squamous epithelia, was identified (in collaboration with A.-H. Hovav et al., Hebrew University, Jerusalem, Israel; Capucha et al., 2018).

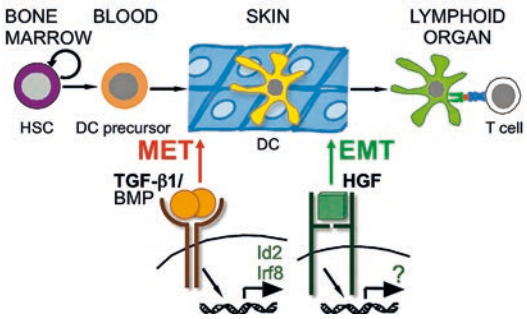


Fig. 4: TGF-β/BMP and HGF receptors are regulators of EMT and MET programs in DC development and migration.

Novel Infrared Cellulose Nanocrystals for Live Cell Imaging

Nanomaterials are highly tunable nanoscale objects, which have received remarkable attention in therapeutic and theragnostic applications. Cellulose nanocrystals (CNC) are a unique and promising natural material extracted from native cellulose. Due to their special surface chemistry, low toxicological risk, negligible inflammatory response and the ability to penetrate cells, CNC are promising candidates for biomedical applications. In this context, nanocellulose-based imaging probes have received considerable attention in recent years. However, CNC with near-infrared (NIR; λ=750-1400 nm) probes have not been reported to date. Higher tissue penetration, lower biological auto-fluorescence and reduced light scattering have greatly increased the interest of NIR fluorescent probes. Known limitations of these probes include dye aggregation, low solubility in water and undesired changes of photophysical properties. Thus, only a limited number of NIR dyes are available, most of them being not easily functionalized and too expensive.

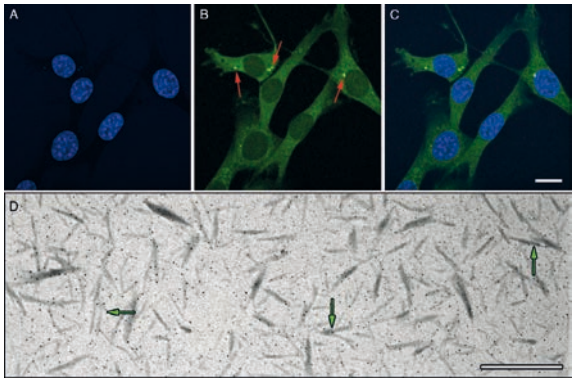


Fig. 5: Imaging of near-infrared cellulose nanocrystals (NIR-CNC). (A-C) Confocal imaging showing NIR-CNC (arrows) internalized by NIH-3T3 cells. Nuclei were stained with DAPI. Scale bar: 15 µm. (D) Transmission electron microscopy analysis of NIR-CNC showing their typical needle-like structure (arrows). Scale bar: 500 nm

To overcome these limitations, we are working on a joint project with Luiz H.C. Mattoso (LNNA, Embrapa Instrumentation, São Carlos, Brazil) centered on the development of near-infrared cellulose nanocrystals (NIR-CNC). NIR-CNC are fabricated via the covalent functionalization of water-soluble perylenediimide based NIR dyes on the surface of the CNC. Physical and chemical characterization of NIR-CNC is done by FT-IR, X-ray diffraction, scanning electron microscopy and X-ray photoelectron spectroscopy. Furthermore, live cell imaging studies (i.e., confocal laser scanning and total internal reflection fluorescence microscopy) are performed to determine the biocompatibility and suitability for short and long-term bioimaging (Fig. 5).

Epigenetic Age-Predictor for Mice

Specific cytosine residues of our DNA become either methylated or demethylated upon aging. It is yet unclear how these epigenetic modifications are governed, but they provide a very powerful biomarker to estimate the age of human donors. More importantly, the deviation between predicted and chronological age was shown to be affected by parameters that influence the aging process, indicating that epigenetic age is indicative of biological age. More recently, several groups described epigenetic age-predictors for mice based on genome wide deep sequencing data. These studies have raised a lot of attention because they facilitate assessment of age-intervention strategies in the murine model. However, the methods based on deep sequencing are relatively labor-intensive and cost-intensive and cannot be easily applied to large cohorts of mice.

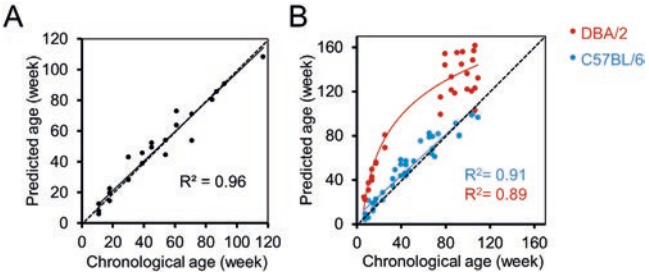


Fig. 6: (A) Three CpG multivariable epigenetic age-predictor for C57BL/6 mice. (B) Epigenetic age-predictions using the three CpG multivariable age-predictor for the C57BL/6 mice (blue) and DBA/2 mice (red) (Han et al., 2018).

Our group has described a bisulfite pyrosequencing approach to analyze the DNA methylation level at only three specific genomic sites in blood samples of mice (Fig. 6A). Notably, epigenetic aging varies between mouse strains and it is accelerated in DBA/2 strain with shorter life expectancy (Fig. 6B). The site-specific DNA methylation analysis at only three CpGs provides an easily applicable tool to further analyze how epigenetic aging is affected in knockout mice or in longevity intervention studies in mice (Han et al., 2018).

Does Soft Really Matter? Differentiation of Induced Pluripotent Stem Cells Towards Mesenchymal Stromal Cells on Soft Gels

Due to their functional plasticity MSC are very important for regenerative medicine, and they are studied in many clinical trials. However, primary MSC isolated from human tissue are very limited in cell numbers, they are highly heterogeneous and difficult to standardize. Therefore, alternative strategies have evolved to derive MSC from iPS cells (iMSC). However, the differentiation of iPS cells towards MSC remains incomplete. It has been suggested that mechanical cues can direct lineage-specific differentiation of stem cells and that particularly matrix elasticity is important for cell fate decisions.

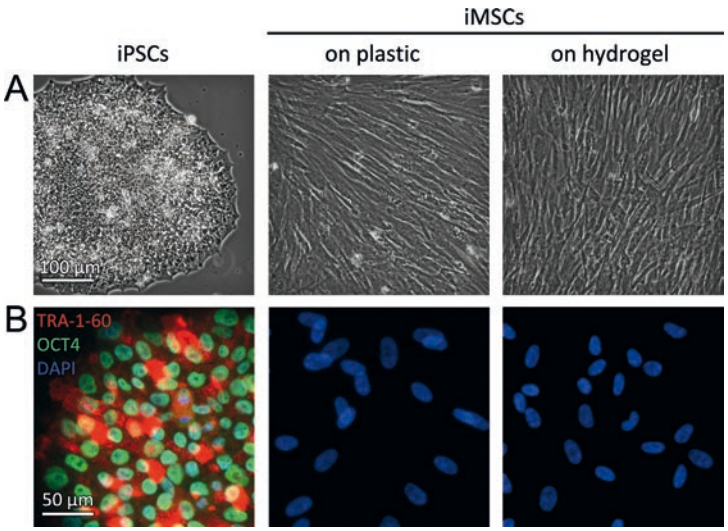


Fig. 7: iPS cells can be differentiated towards MSC on stiff plastic and on soft hydrogel. (A) After 35 days of differentiation, iMSC demonstrated MSC-like morphology. (B) The pluripotency markers TRA-1-60 (red) and OCT4 (green) were downregulated during differentiation (nuclei stained with DAPI, blue) (Goetzke et al., 2018).

We demonstrate that iPS cells can be effectively differentiated towards MSCs on fibrin-based hydrogels (Fig. 7; Goetzke et al., 2018). Unexpectedly, this complex differentiation process is not affected by the soft substrate: iMSC generated on plastic or hydrogel have the same morphology, immunophenotype, differentiation potential, and gene expression profiles. Moreover, global DNA methylation patterns of iMSC generated on plastic or hydrogel indicate that they are epigenetically alike. These findings add to recent controversy if and how mechanical stimulation impacts on cellular differentiation.

Acknowledgements

This work was supported by:

- German Research Foundation (DFG)
- German Federal Ministry of Education and Research (BMBF)
- Deutsche Krebshilfe
- European Union (EU)
- Interdisciplinary Centre for Clinical Research Aachen (IZKF Aachen)
- Exploratory Research Space (ERS)
- Else-Kröner-Fresenius Foundation
- Donation by U. Lehmann
- Donation by Vision4 Life Sciences
- StemCellFactory is co-funded by the European Union (European Regional Development Fund - Investing in your future) and the German Federal State North Rhine-Westphalia (NRW)

Selected References in 2018

[1] Božić, T., Frobel, J., Raic, A., Ticconi, F., Kuo, C.C., Heilmann-Heimbach, S., Goecke, T.W., Zenke, M., Jost, E., Costa, I.G. and Wagner, W. (2018). Variants of DNMT3A cause transcript-specific DNA methylation patterns and affect hematopoiesis. Life Sci. Alliance, 1(6):e201800153.

[2] Capucha, T., Koren, N., Nassar, M., Heyman, O., Nir, T., Levy, M., Zilberman-Schapira, G., Zelentova, K., Eli-Berchoer, L., Zenke, M., Hieronymus, T., Wilensky, A., Bercovier, H., Elinav, E., Clausen, B.E., and Hovav, A.-H. (2018). Sequential BMP7/TGF-β1 signaling and microbiota instruct mucosal Langerhans cell differentiation. J. Exp. Med. 215, 481-500.

[3] Chteinberg, E., Rennspiess, D., Sambo, R., Tauchmann, S., Kelleners-Smeets, N.W.J., Winnepenninckx, V., Speel, E.J., Kurz, A.K., Zenke, M., and zur Hausen, A. (2018a). Phosphatidyinositol 3-kinase p110δ expression in Merkel cell carcinoma. Oncotarget 9, 29565-29573.

[4] Chteinberg, E., Sauer, C.M., Rennspiess, D., Beumers, L., Schiffelers, L., Eben, J., Haugg, A., Winnepenninckx, V., Kurz, A.K., Speel, E.J., Zenke, M., and zur Hausen, A. (2018b). Neuroendocrine key regulator gene expression in Merkel cell Carcinoma. Neoplasia 12, 1227-1235.

[5] Cypris, O., Frobel, J., Rai, S., Franzen, J., Sontag, S., Goetzke, R., Toledo, M.A.S., Zenke, M., and Wagner, W. (2018). Tracking of epigenetic changes during hematopoietic differentiation of induced pluripotent stem cells. Clin. Epigenetics, in press.

[6] Drescher, H.K., Schumacher, F., Schenker, T., Baues, M., Lammers, T., Hieronymus, T., Trautwein, C., Streetz, K.L., and Kroy, D.C. (2018). C-Met signaling protects from nonalcoholic steatohepatitis- (NASH-) induced fibrosis in different liver cell types. Oxid. Med. Cell Longev., 6957497.

[7] Fernandez-Rebollo, E., Eipel, M., Seefried, L., Hoffmann, P., Strathmann, K., Jakob, F., and Wagner, W. (2018). Primary osteoporosis is not reflected by disease-specific DNA. J. Bone Miner. Res. 33, 356-361.

[8] Frank, S., Ahuja, G., Bartsch, D., Russ, N., Yao, W., Kuo, C.C., Derks, J.P., Akhade, V.S., Kargapolova, Y., Georgomanolis, T., Messling, J.E., Gramm, M., Brant, L., Rehimi, R., Vargas, N.E., Kuroczik, A., Yang, T.P., Sahito R.G.A., Franzen, J., Hescheler, J., Sachinidis, A., Peifer, M., Rada-Iglesias, A., Kanduri, M., Costa, I.G., Kanduri, C., Papantonis, A., and Kurian, L. (2018). yylncT defines a class of divergently transcribed lncRNAs and safeguards the T-mediated mesodermal commitment of human PSCs. Cell Stem Cell, Nov 21, Epub ahead of print.

[9] Frobel, J., Bozic, T., Lenz, M., Uciechowski, P., Han, Y., Herwartz, R., Strathmann, K., Isfort, S., Panse, J., Esser, A., Birkhofer, C., Gerstenmaier, U., Kraus, T., Rink, L., Koschmieder, S., and Wagner W. (2018). Leukocyte counts based on DNA methylation at individual cytosines. Clin. Chemistry 64, 566-575.

[10] Frobel, J., Rahmig, S., Franzen, J., Waskow, C., and Wagner W. (2018). Epigenetic aging of human hematopoietic cells is not accelerated upon transplantation into mice. Clin. Epigenetics 10, 67.

[11] Göbel, C., Goetzke, R., Eggermann, T., and Wagner W. (2018). Interrupted reprogramming into induced pluripotent stem cells does not rejuvenate human mesenchymal stromal cells. Sci. Rep. 8, 11676.

[12] Goetzke, R., Franzen, J., Ostrowska, A., Vogt, M., Blaeser, A., Klein, G., Rath, B., Fischer, H., Zenke, M., and Wagner, W. (2018). Does soft really matter? Differentiation of induced pluripotent stem cells into mesenchymal stromal cells is not influenced by soft hydrogels. Biomaterials 156, 147-158.

[13] Goetzke, R., Sechi, A., De Laporte, L., Neuss, S., and Wagner, W. (2018). Why the impact of mechanical stimuli on stem cells remains a challenge. Cell Mol. Life Sci. 75, 3297-3312.

[14] Grezella, C., Fernandez-Rebollo, E., Franzen, J., Ventura Ferreira, M.S., Beier, F., and Wagner W. (2018). Effects of senolytic drugs on human mesenchymal stromal cells. Stem Cell Res. Ther. 9, 108.

[15] Han, Y., Eipel, M., Franzen, J., Sakk, V., Dethmers-Ausema, B., Yndriago, L., Izeta, A., de Haan, G., Geiger, H., and Wagner W. (2018). Epigenetic age-predictor for mice based on three CpG sites. Elife 7, pii: e37462.

[16] Jakob, F., Ebert, R., Fernandez-Rebollo, E., Bischof, O., and Wagner W. (2018). Response to letter to the editor of JBMR: Epigenetic aging in osteoporosis. J. Bone Miner. Res. 33, 1904-1905.

[17] Li, J., Garcia, C.C., Riedt, T., Brandes, M., Szczepanski, S., Bossart, P., Wagner, W., and Janzen, V. (2018). Murine hematopoietic stem cell reconstitution potential is maintained by osteopontin during aging. Sci. Rep. 8, 2833.

[18] Li, Z., Schulz, M.H., Look, T., Begemann, M., Zenke, M., and Costa, I.G. (2018). Identification of transcription factor binding sites using ATAC-seq. Genome Biol., in press.

[19] Lubberich, R.K., Walenda, T., Goecke, T.W., Strathmann, K., Isfort, S., Brümmendorf, T.H., Koschmieder, S., and Wagner, W. (2018). Serum of myeloproliferative neoplasms stimulates hematopoietic stem and progenitor cells. PLoS ONE 13, e0197233.

[20] Malik, A., Meyr, U., Herfs, W., Zenke, M., and Wanek, P. (2018). Control of dynamically inherent biological processing in cell technology – Adaptive strategies for automated cell culture. 2018 IEEE International Conference on Engineering, Technology and Innovation (ICE/ITMC).

[21] Marioni, R., Belsky, D.W., Deary, I.J., and Wagner, W. (2018). Association of facial aging with DNA methylation and epigenetic age predictions. Clin. Epigenetics 10, 140.

[22] Meents, J.E., Bressan, E., Sontag, S., Foerster, A., Hautvast, P., Rösseler, C., Hampl, M., Schüler, H., Goetzke, R., Le, T.K.C., Kleggeteveit, I.P., Cann, K.L., Rush, A.M., Rogers, M., Kohl, Z., Schmelz, M., Wagner, W., Jørum, E., Namer, B., Winner, B., Zenke, M., and Lampert, A. (2018). The role of Nav1.7 in human nociceptors: insights from human iPS cell-derived sensory neurons of erythromelalgia patients. Pain, in press.

[23] Oberacker, T., Bajorat, J., Ziola, S., Schroeder, A., Röth, D., Kastl, L., Edgar, B.A., Wagner, W., Gülow, K., Krammer, P.H. (2018). Enhanced expression of thioredoxin-interacting-protein regulates oxidative DNA damage and aging. FEBS Lett. 592, 2297-2307.

[24] Sagi, Z., and Hieronymus, T. (2018). The Impact of the epithelial-mesenchymal transition regulator hepatocyte growth factor receptor/Met on skin immunity by modulating Langerhans cell migration. Front. Immunol. 9, 517.

[25] Schmidt, E., Dhaouadi, I., Gaziano, I., Oliverio, M., Klemm, P., Awazawa, M., Mitterer, G., Fernandez-Rebollo, E., Pardas-Juni, M., Wagner, W., Hammerschmidt, P., Loureiro, R., Kiefer, C.A., Hansmeier, N.R., Khani, S., Bergami, B., Heine, M., Ntini, E., Frommolt, P., Zentis, P., Ørom, U., Heeren, J., Blüher, M., Bilban, M., and Kornfeld, J.W. (2018). LincRNA H19 protects from dietary obesity by constraining expression of monoallelic genes in brown fat. Nat. Commun. 9, 3622.

[26] Schultz, K., Grieger (Lindner), C., Li, Y., Urbánek, P., Ruschel, A., Minnich, K., Bruder, D., Gereke, M., Sechi, A. and Herrlich, P. (2018). Gamma secretase dependent release of the CD44 cytoplasmic tail upregulates IFI16 in cd44-/- tumor cells, MEFs and macrophages. PLoS One 13, e0207358.

[27] Sheng, C., Jungverdorben, J., Wiethoff, H., Lin, Q., Flitsch, L., Ekkert, D., Hebisch, M., Fischer, J., Kevasan, J., Weykopf, B., Schneider, L., Holtkamp, D., Beck, H., Till, A., Wuellner, U., Ziller, M., Wagner, W., Peitz, M., Brüstle, O. (2018). A stably self-renewing adult blood-derived induced neural stem cell exhibiting patternability and epigenetic rejuvenation. Nat. Commun. 9, 4047.

[28] Zenke, M., Marx-Stölting, L., and Schickl, H., Editors (2018). Stem Cell Research – Current scientific and societal developments. Nomos Publisher, Baden-Baden, Germany.

[29] Zirkel, A., Nikolic, M., Sofiadis, K., Mallm, J.-P., Brackley, C.A., Gothe, H., Drechsel, O., Becker, C., Altmüller, J., Josipovic, N., Georgomanolis, T., Brant, L., Franzen, J., Koker, M., Gusmao, E.G., Costa, I.G., Ullrich, R.T., Wagner, W., Roulos, V., Nürnberg, P., Marenduzzo, D., Rippe, K., and Papantonis, A. (2018). HMGB2 loss upon senescence entry disrupts genomic organization and induces CTCF clustering across cell types. Mol. Cell 7, 1-15.

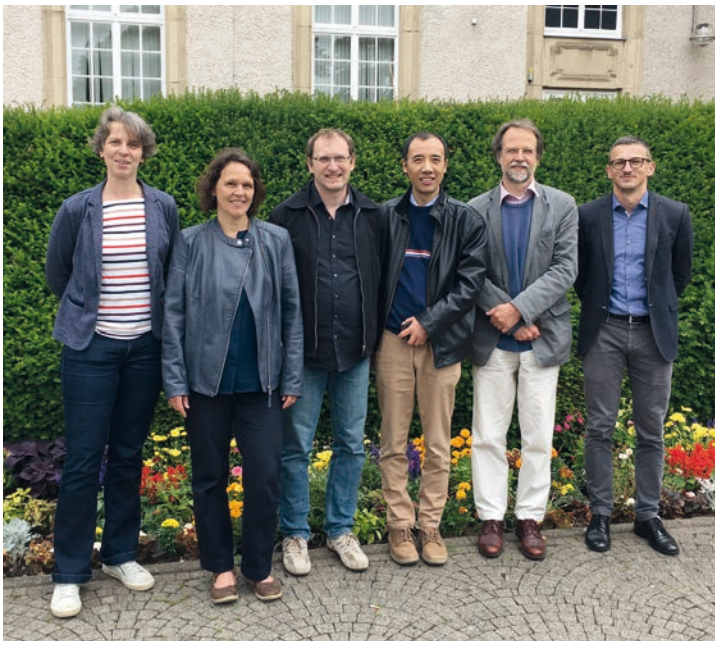
[30] Synthetische Biologie, Standortbestimmung. Positionspapier der Ständigen Senatskommission für Grundsatzfragen der Genforschung, 2018.

[31] Translation – von der Stammzelle zur innovativen Therapie. Analyse und Empfehlungen zur klinischen Translation von Stammzellforschung in Deutschland. White Paper des German Stem Cell Networks, Arbeitsgruppe Translation stammzellbasierter Therapien, 2018.

Team

Lab retreat in The Hague, Netherlands.

Stephanie Sontag, PhD, speaking to Professor Emmanuelle Charpentier, recipient of Aachen Engineering Award 2018, at the RWTH Aachen Graduation Celebration 2018.



Small lab reunion at the occasion of the 15th International Symposium on DC (DC2018) in Aachen, Germany. Kristin Seré, PhD, RWTH Aachen University; Sandra Diebold, PhD, National Institute for Biological Standards and Control (NIBSC), Hertfordshire, UK; Thomas Hieronymus, PhD, RWTH Aachen University; Xinsheng Ju, PhD, ANZAC Research Institute, Sydney, Australia; Martin Zenke, PhD, Professor, RWTH Aachen University; Nicolas Goncharenko, PhD, Institut National de Cancer, Luxembourg (from left to right).