HELENA
Helmholtz Graduate School Environmental Health

GSISH TUM
Graduate School of Information Science in Health

Outline of the Course

The 15th edition of the Spring School of Bioinformatics for Molecular Biologists will be held from 21st through 25th March 2015. It is organized by the Institute of Bioinformatics and Systems Biology of the Helmholtz Centre München (IBIS). The course is part of the HMGU Ph.D. programme (Graduate School) but also open to other Ph.D. students and post-graduates.

This year's course aims for an introduction to the challenges and promises of personalized medicine. Given the data, can we arrive at precise advice for successful therapies? For complex diseases such as diabetes or schizophrenia, can we identify causes and optimize therapies? How to interpret data from the gut microbiome? And, how can experimentalists and bioinformaticians collaborate on complex problems such as nuclear receptors? What are the foundations of tackling complex biology and genetics and what systems biology and bioinformatics can contribute to the translation of basic research into the clinic? These are some topics that will be addressed in the course lectures.

Our society is driven by information, making humans a unique species mastering exchange, storage and analysis of data. Language and writing, data collection and networking are cornerstones of the intellectual and economic evolution. From the Stone Age to the present day instant access to more information than any individual can ever digest.

The reality of life science research is caught by the contradiction of the enormous power of data generating experiments and the need to arrive at clear-cut solutions for pressing needs of an ageing society in the industrial countries on the one hand and the bare necessity to cope with the needs of a fast growing population in the third world.

Personalized medicine describes a paradigm that is far from being well defined. At least, it aims for a structured approach to distinguish the (disease) state from one individual to another. But is the knowledge that a certain allele of gene A increases the risk for disease B sufficient to improve the success of the therapy, to avoid complications, and to increase the efficiency of the health care system?

Even a simple biological system such as a prokaryotic cell consists of thousands of variables describing the cellular information. Far more complex in multicellular organism, genetics, regulatory processes, as well as the environment conditionally influence the disease phenotype. To answer any question about function and malfunction of biological systems requires not only the observation of data but also the interpretation in context of any related biological knowledge.

Bioinformatics and Computational Biology have built an arsenal of methods, tools and data resources available to the scientific community. However, two main problems persist and handicap the interdisciplinary collaboration between the experimentalists and the bioinformaticians: understanding the principles and the limitations of the computational methods on the one hand and, on the other, realizing that data analysis is not a black box that returns something "ready for publication" after the experiment has generated some data.

The Spring School gears for the understanding of concepts and how

these can be applied in practice. What is the role of algorithms, models, and biological knowledge? Why do we need network analysis and what are the main tools required for generating our next publication?

The future of medicine will be data driven. Insight into disease mechanisms has to be translated into practical decision support for medical doctors. The course will foster interdisciplinary ideas and stimulate discussion between experts and students. An open discussion on the world of data we live in and how we will perform our work in the future in distributed teams will be part of the course.

Expert faculty members will introduce the basics in tutorials but also discuss new developments in the interdisciplinary fields related to human disease. The course asks for your active participation, the faculty members will be ready to discuss your projects and ideas face to face. The course is tailored for Molecular Biologists and aims to support the important dialogue between the experimentalist interested in a specific biological problem and the theoretician eager to solve problems in a generic, reusable way.

The course aims to provide a head start in this important interdisciplinary field by presenting basic concepts as well as recent applications. The intended audience are Ph.D. students and junior scientists. Its main subjects will be the integration of information, biological networks, and concepts in Systems Biology. The course is supported by the Helmholtz Graduate School (HELENA).

H. Werner Mewes

HMGU, Inst. f. Bioinformatics and Systems Biology
TUM Chair f. Bioinformatics, Center for Life and Food Science, Weihenstephan

Prerequisites for participation:
Participants should have some very basic knowledge in bioinformatics such as sequence comparison. There are no formal requirements.

Fee and registration:
€ 700 (including tuition, course material, room and board for the whole duration of the event, bus transfer from Munich/Neuherberg to Bertinoro). The course fee for HELENA Graduate School students will be covered by the respective Graduate School.

Registration:
Please register as soon as possible since the number of available places is limited (30)! Please distribute this invitation to all interested Ph.D. students and young scientists.

For **reservations please contact** the Secretariat of the Helmholtz-Institute for Bioinformatics and Systems Biology (ibis.office@helmholtz-muenchen.de).

Location: Bertinoro, Italy (close to Forli, about 40 km from Bologna)

Transport: A bus will be organized from Munich to Bertinoro leaving Neuherberg in the morning of the 21st of March.

Course Schedule and additional information:

See http://www.helmholtz-muenchen.de/en/mips/events/

DIRECTOR:

Prof. Dr. H.W. Mewes (Helmholtz Zentrum München and TU München)

Lecturers and Topics

Lecturer	Affiliation	Topic
M. Campillos	Helmholtz Zentrum München (HMGU)	Pharmacogenomics
L.J. Jensen	Univ. Kopenhagen, Panum Inst.	Large-scale integration of data and text for medicine
K. Haase	Technische Univ. München	Individual Cancer Genetics
G. Kastenmüller	HMGU	Metabolomics for Personalized Medicine
J. Krumsiek	HMGU, CMB	Systems Biology and Models
R. Küffner	HMGU	Transcriptional Biological Networks
H.W. Mewes	Technische Univ. München & HMGU	Principles of causality Systems Biology and Individualized Medicine
A. Pfeufer	HMGU	Human Genetics
H. Prokisch	HMGU/TUM	Genetics of rare mitochondrial diseases
T. Rattei	Univ. Vienna	Metagenomics is individual
D. Rujescu	Univ. Halle	Genetics of Psychiatric diseases
H. Uhlenhaut/ D. Boyanova	Helmholtz Zentrum München	Nuclear Receptors from Experiment to Genetic Variation
T. Werner	Univ. of Michingan, Ann Arbor	Translational Transcriptomics

Bioinformatics Spring School
21.03 – 25.03. Preliminary Schedule

Saturday, 21. 03.
Arrival Bertinoro

Sunday, 22. 03.

9:00 – 10:00	H.W. Mewes	Introduction to the Course Presentation of the Faculty Presentation of the Participants
10:30 – 12:30	T. Rattei	Metagenomics is individual
13:30 – 15:00	D. Rujescu	Genomics in Psychiatric Diseases
15:30 – 17:00	L.J. Jensen	Large-scale integration of data and text

Monday, 23. 03.

8:30 – 10:30	H. Uhlenhaut / D. Boyanova	Nuclear Receptors
11:00 – 12:30	G. Kastenmüller	Metabolomics for individual genetics
13:30 – 15:00	H. Prokisch	Mitochondrial Diseases
15:15 – 16:45	M. Campillos	Pharmacogenetics
17:00 – 18:30	A. Pfeufer	Deciphering genomics

Tuesday, 24. 03.

9:00 – 10:30	H.W. Mewes	Epistemology and Personalized Medicine
11:00 – 12:30	R. Küffner	Regulatory Networks
13:30 – 15:00	H.W. Mewes	Systems Biology of Diseases
15:30 – 17:00	K. Haase	Cancer Genetics
17:00 – 18:30	T. Werner	Translational Transcriptomics

Wednesday, 25. 03.

09:00 - 11:00	J. Krumsiek	Quantitative Models and Simulation for Systems Biology
11:15 - 12:00	H.W. Mewes	Final Roundtable
13:00	Departure	

Faculty members of the 15th Course on Bioinformatics and Systems Biology

Prof. Dr. H.W. Mewes,
TU München & Helmholtz Zentrum München

Professor for Bioinformatics at the TU München, Weihenstephan and Head of the Inst. f. Bioinformatics and Systems Biology at the Helmholtz-Zentrum München. Educated as a chemist (Univ. Marburg) he worked in bioenergetics at the Univ. of Heidelberg, in protein chemistry at the EMBL and joined the Max-Planck-Inst. f. Biochemistry in 1985. From 1988 he led the MIPS group active in data collection for protein sequences and genome analysis (yeast, A. thaliana). He has initiated curriculum in bioinformatics started in 2001 as a joint activity of LMU and TUM. He is Co-Founder of Biomax Informatics (1997) and Clueda (2012).

Main interests: genome analysis, human genotype vs. disease biology, qualitative models and knowledge representation, philosophy of (life)-science.

Epistemology of Personalized Medicine:
Why death is unavoidable? Why is it so difficult to predict the onset and progress of a disease? Disease oriented and clinical research aim to find disease mechanisms using all kinds of approaches and technologies from Randomized Control Trials to patient-derived IPS cells. The recent development of high-dimensional data generation based on omics-technologies marks a transition from individual, hypothesis driven discovery to systemic investigation without fixing any hypothesis at the beginning of the observation. Epistemology is needed for the critical evaluation of our methods applied. The gene/environment concept involves thousands of variables generated by genetic variance, ageing, and everything that we can subsume as “environment”, namely nutrition, life style, drugs, exercise, stress and all other physical, chemical, and mental factors we interact with. How we deal with complex systems comprising trillions of cells that can have more states than there are molecules in the universe, how we can achieve prediction and gain control to cure diseases is very much a methodological challenge. The lecture will touch some of the underlying principles of science such as causality and complexity with emphasis on Personalized Medicine.

Systems Biology of Diseases: Diseases represent a fundamental concept of human health care. A huge classification scheme documented in sophisticated collections such as IDC10 and DSM-V are based on phenotypic evidence but not on biological causes. Only recently rationale insight into disease aitioloy based on genetic and functional molecular information became feasible. This development has substantially changed research concepts, publications and the perspectives for individual treatment in the future. I will discuss how Systems Biology and its applications might help to translate knowledge into health care.

Dr. Monica Campillos, Helmholtz Zentrum München

Junior Group Leader at the Institute of Bioinformatics and Systems Biology, Helmholtz Zentrum München. Main interest: chemical-protein networks, chemical-disease networks, drug discovery, integration and analysis of biological information of small molecules.

Pharmacogenetics

Pharmacogenetics is a newly evolving field that studies the impact of genetic variants on drug efficacy and adverse effects. In this lecture, I will present an overview of the state of the art of this field including a current list of clinical and suspected associations between genetic polymorphisms and drug response and adverse effects. I will also revise the genetic and computational approaches to detect pharmacogenomic associations, their limitations and challenges. Special attention will be paid to pharmacogenetics of cancer, where a large number of these analyses have been performed in the recent years. Finally, I will talk about resources and datasets containing pharmacogenetics information.

Kerstin Haase, Technische Universität München

Kerstin Haase studied Bioinformatics at the Technical University and Ludwig-Maximilians-University in Munich and obtained her Diploma in 2011.

Since then she is a PhD student in Prof. Frishmans group in Weihenstephan working on the application of next generation sequencing in the fields of virology and oncology. Her current work focuses on intraindividual virus evolution and the expression of endogenous virus elements in mammary and urothel carcinomas.

Cancer Genetics

The development of human tumours relies on overcoming different control mechanisms, which regulate cell growth, division and death in normal tissues. These steps towards malignancy have been described as the “hallmarks of cancer” and will be discussed in detail.

Analysis of cancer genomes is made difficult by the heterogeneity of the tumour subpopulations that can also influence the response to therapies. With the rise of whole genome sequencing, these subpopulation dynamics can be analysed in detail and individual clonal relationships identified. The talk will cover bioinformatics approaches that aim at examining the different tumour cell populations, their phylogenetic relationships and the identification of driver mutations during cancer progression.

Prof. Lars Juhl Jensen, Panum Inst. Copenhagen

Lars Juhl Jensen started his research career in Søren Brunak's group at the Technical University of Denmark (DTU), from which he in 2002 received the Ph.D. degree in bioinformatics for his work on non-homology based protein function prediction. During this time, he also developed methods for visualization of microbial genomes, pattern recognition in promoter regions, and microarray analysis. From 2003 to 2008, he was at the European Molecular Biology Laboratory (EMBL) where he worked on literature mining, integration of large-scale experimental datasets, and analysis of biological interaction networks. Since the beginning of 2009, he has continued this line of research as a professor at the Novo Nordisk Foundation Center for Protein Research at the Panum Institute in Copenhagen and as a co-founder and scientific advisor of Intomics A/S. He is a co-author of more than 100 scientific publications that have in total received more than 10,000 citations.

Large-scale integration of data and text

High-throughput technologies such as DNA sequencing, microarrays, mass spectrometry, and protein interaction assays have resulted in an ever-increasing flood of data. To make the most of such data sets, it is important to integrate them both with each other and with the existing scientific literature. In my presentation, I will explain how heterogeneous data types are integrated in STRING to construct a network of functional associations. I will also introduce STITCH, which extends STRING with protein-chemical interactions as well as a suite of three new web-based resources that use similar techniques, including text mining, to associate the proteins in the STRING network with cellular compartments, tissues, and diseases. Finally, I will talk about how we currently apply similar techniques to mine data and text from electronic health records and registries to analyze temporal trajectories of diseases and adverse reactions of drugs.

Dr. Robert Küffner,
Helmholtz Zentrum München

Robert Küffner is a group leader and lecturer currently at the Helmholtz Zentrum München. He habilitated in informatics in 2010 and has been, since 2003, orking in the computer science and bioinformatics department at the Ludwig-Maximilians Universität München, Germany. Between the years 2000 and 2003, he was head of software development at the National Center for Genome Resources (NCGR) in New Mexico, USA. He received his PhD in molecular biology in 1998 at the Heinrich-Heine Universität Düsseldorf, Germany. Küffner's main interests include the investigation and reconstruction of biological networks via Petri Nets as well as research in the areas of text mining, expression analysis, gene regulation, and systems biology. Approaches and tools resulting from this research have been applied in many projects to provide systematic bioinformatics support; e.g. for the pre-processing, analysis and integration of large-scale transcriptomics and proteomics datasets. Recently, his team was recognized as best performer in two international community-wide challenges where comprehensive blinded assessments of network inference approaches have been conducted. He is also challenge organizer, for instance aiming at the prediction of disease progression of Amyotrophic lateral sclerosis (ALS) patients.

Regulatory Networks: Regulatory networks are invaluable to integrate and interpret the results from heterogeneous experiments. The systemic implications from genetic or other defects can only be understood in the context of networks. However, current experimentally supported regulatory networks are far from complete, so their complementation from mRNA expression data is an important but difficult problem. Available approaches are characterized by their specific performances, data requirements, and inherent biases. The so far largest assessments of inference approaches has been conducted via recent community-wide challenges, the Dialogue on Reverse Engineering Assessment and Methods (DREAM). Predictions are evaluated against experimentally supported interactions in procaryote and eukaryote model organisms. Our analyses revealed limitations of the current methods, for instance that gene expression data alone is insufficient to understand the regulatory circuitries. Required additional experiments can for instance be obtained from the ENCODE project that aimed to identify all regions in the genome sequence relevant for transcription, transcription factor association, chromatin structure and histone modification.

Jan Krumsiek, Helmholtz Zentrum München

Jan Krumsiek studied Bioinformatics at the TU Munich and LMU Munich, receiving his diploma in 2009. He obtained his PhD in Bioinformatics from the TU Munich in 2012, working on network methods for metabolomics data at the Institute of Bioinformatics and Systems Biology (IBIS), Helmholtz Zentrum München. From 2012 to 2013, he worked as a Postdoctoral Fellow at the IBIS. Since 2013, he leads the 'Systems Metabolomics' research team at the Institute of Computational Biology, Helmholtz Zentrum München. Moreover, he is a visiting fellow at the Weill Cornell Medical College, New York City, USA.

Quantitative models and simulation for Systems Biology

In Systems Biology, experimentalists and theoreticians make a concerted effort to unravel the functionality of complex biological systems: Experimental knowledge allows the creation and refinement of mathematical models, which, in turn, help to design and optimize further experiments. In this talk we will go through basic principles of mathematical modeling, covering differential equations, mass-action kinetics, enzyme-catalyzed reactions, stability analysis, discrete modeling approaches, network biology and biostatistics. We will discuss all methods in the context of real biological examples like, for example, stem cell differentiation mechanisms and metabolomics measurements.

Dr. Gabi Kastenmüller, Helmholtz Zentrum München

Dr. Kastenmüller holds a master's degree in chemistry and a master's degree in computer science from the Ludwig-Maximilians Universität München. In 2009, she obtained her PhD in Bioinformatics from the Technische Universität München for her work on *in silico* prediction and comparison of metabolic capabilities from sequenced genomes. In the same year, she joined Karsten Suhre's group focusing on metabolomics at the Institute of Bioinformatics and Systems Biology (IBIS), Helmholtz Zentrum München, where she was involved in the analysis of various large-scale metabolomics experiments. In 2010, she spent four months at the metabolomics company Metabolon, Inc, USA as a visiting scientist, delving into metabolite identification and the interpretation of spectral data. Since 2011, she has headed the Metabolomics Group at IBIS. Her group mainly focuses on the analysis and interpretation of high-throughput metabolomics data sets by the means of bioinformatics and systems biology. In particular, they are interested in the inborn metabolic individuality in human populations and how this individuality affects predisposition to diseases and response to treatments.

Metabolomics
is the systematic study of ideally all small molecules (metabolites) in a biological system such as a cell, tissue, or a complete organism. In contrast to genomics, transcriptomics, and proteomics, metabolomics describes the end point of all regulatory and enzymatic processes in a biological system, which is influenced by genetic and environmental factors. The metabolite profile of a system thus represents a snapshot of its physiological state.

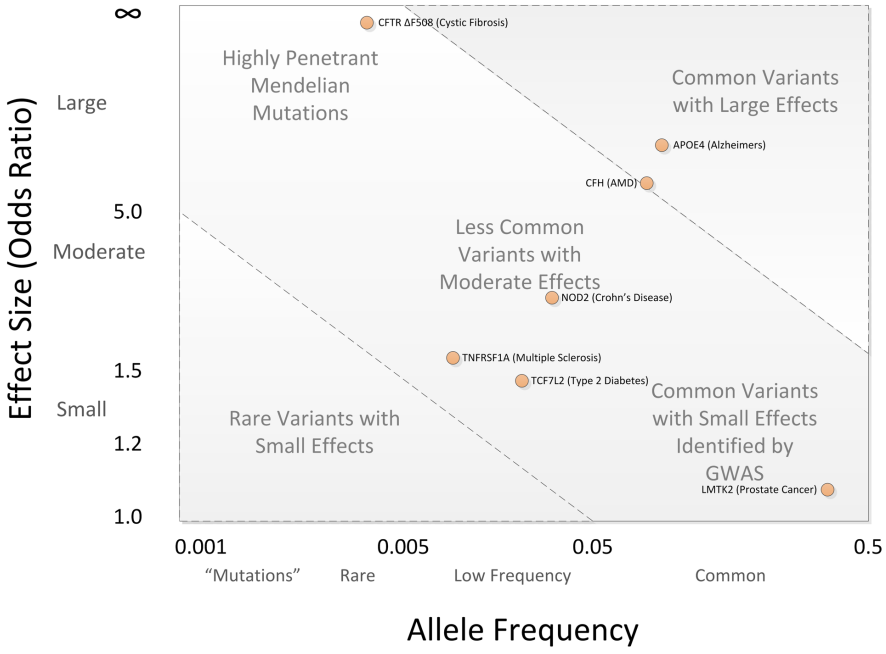
In my talk, I will first introduce the different approaches that are currently used for quantifying small organic molecules in a high-throughput metabolomics setting. Subsequently, I will give an overview of all steps in the analysis of data produced by these approaches. Finally, we will go through selected examples of current metabolomics projects allowing the participants to find out how metabolomics may be useful for their own research.

PD Dr. Arne Pfeufer, HMGU and TU München

Arne Pfeufer, MD, MSc obtained his M.S. in biochemistry in 1992 at Hannover University and his medical degree in 1997 at Humboldt University Berlin. In his medical thesis he characterized causal and modifier genes in hypertrophic cardiomyopathy, a monogenic heart disease. Between 1998 and 2000 he did residency training in internal medicine at the Charité in Berlin and the Kerckhoff-Klinik in Bad Nauheim. In 2001 he started his specialty training in human genetics at the Department of Human Genetics at the Klinikum Rechts der Isar of TU München and at the Helmholtz Zentrum München ((HMGU). There he shifted his scientific interest more towards common genetic determinants of quantitative cardiac traits and common heart diseases. In 2008 he was board certified in human genetics and in 2011 appointed lecturer in human genetics at the TU München. In 2012 he became group leader for predictive and preventive medicine at the Institute for Bioinformatics (IBIS) of the Helmholtz Zentrum München. He continues to work on the same topics including patient and population based studies of cardiovascular disease risk with a special focus on translation of research findings into prediction and prevention.

"Deciphering Genetics: How to distinguish between "genetic causes" and "genetic risk factors" for disease ?"

Genetic predisposition to disease comprises both high effect low allele frequency genome variants (i.e. rare mutations in monogenic diseases) as well as low effect high allele frequency genome variants (i.e. common predisposing polymorphisms). In fact according to Sewall Wright (1889-1988) these are just two extreme cases of the distribution of genome variants plotted by effect size vs. allele frequency.



Rare mutations in monogenic disorders have traditionally been identified by linkage analysis, which is now being replaced by next generation sequencing technology. Common polymorphisms increasing

the risk for complex disorders such as heart disease, cancer, diabetes, asthma, and stroke have been identified by genome-wide association studies ("GWAS") since 2005 with great success.

In this session we will unite the views of bioinformatics, human genetics, genetic epidemiology, statistics and test theory on the subject of genetic predispositions to disease We will discuss concepts from all these fields such as causality, heritability, penetrance, population attributable risk, positive and negative predictive value etc. in order to obtain a holistic, united and comprehensive view on the subject.

We will also discuss how to translate genetic predispositions into novel diagnostic and predictive tests as well as into novel therapies, the systematic implementation of which is known as the "biomedical research cycle".

Dr. Holger Prokisch, Technische Universität München

Holger Prokisch undertook his undergraduate and graduate studies in Germany, first at the Georg-Büchner-Gymnasium, Seelze and then at the Technical University Hannover. After his postdoctoral training at the Institute for Physiological Chemistry, University of Munich, Dr. Prokisch became head of the Biogenesis of Mitochondria research group at the same institute with Prof. W Neupert before attaining his current position as senior scientist and head of the Genetics of Mitochondrial Disorders group at the Institute of Human Genetics of the Technical University Munich. His research focus seeks to understand genetic variation in both rare and common disorders leading to mitochondria-related disease. By applying next generation sequencing the group has contributed to the growing list of genes identified in Mendelian disorders. In his work, Dr. Prokisch undertakes genomic, proteomic, metabolomic, and transcriptomic studies to produce a comprehensive picture of mitochondrial dysfunction **(**http://publicationslist.org/prokisch).

Mitochondrial disorders (mitochondriopathies) are one of the most commonly occurring neurometabolic disorders in children. With molecular-genetic diagnostics of large sets of genes (gene panels, exome sequencing) becoming less expensive, it is expected that they will be increasingly used in clinical practice. This will especially affect those monogenic diseases which are heterogenic, that is, in which mutations of many different genes result in phenotypes that are clinically difficult to distinguish from each other. Respiratory chain defects are an example of such disorders. Exome sequencing allows for rapid, simultaneous screening of all genes that come into question.
In my talk I will introduce the power and limitations of exome sequencing. By going through several examples we will see how important validation experiments are but also the power of combined analysis of several thousand of exome sequencing data. Finally, selected examples will illustrate how the molecular diagnosis lead personalized treatments of patients with mitochondrial disorders.

Prof. Dr. Thomas Rattei, University of Vienna

Professor for Computational Biology and vice-head of the Department of Microbiology and Ecosystem Research at the University of Vienna. Main interest: microbial genomics and systems biology, symbiosis, pathogens and host-microbe interactions, molecular inter-species interactions in diverse ecosystems, strategies for the evaluation of computational methods in biology ,large scale sequence analysis.

Metagenomics is individual

Microbes represent the most diverse and most abundant group of living organisms. Our knowledge about the biology of prokaryotic microorganisms is mainly obtained from a small minority of lab-cultivable species. This also applies to one of the most important microbial communities: the human microbiome. The 16S rRNA approach and whole-genome sequencing of cultivable microbes during the last 20 years have pushed this field substantially, and has helped to establish molecular models of human microbiomes. Applications of this research include fundamental topics such as human health and nutrition. Novel technologies, such as metagenomics and single-cell genomics, are currently extending the scope of microbial genomics towards the majority of uncultivable species. These methods rely on sophisticated computational approaches for assembly, binning and annotation of microbial genomes. This talk will give an overview on the basics, the state-of-the art and the latest developments in this field and will discuss remaining challenges. It will further address the implications of the quickly growing number of automatically assembled, near-complete genomes for genome databases, comparative genomics and systems biology of human microbiomes.

Prof. Dr. Dan Rujescu, Univ. of Halle

Prof. Dr. Dan Rujescu, is actually Chair of the Department of Psychiatry, Psychotherapy and Psychosomatics of the University of Halle, Germany. He received his medical degree from the Universities Heidelberg and Essen. From 1993-1995 he worked as a physician at the Department of Psychiatry of the University of Mainz. Afterwards, he moved to the Department of Psychiatry of the University of Munich where he became Head of the Division of Molecular and Clinical Neurobiology. During his time in Munich he became a senior physician, a medical specialist in psychiatry and psychotherapy, a full Professor for Psychiatry, Head of the Alzheimer Memorial Center, as well as Deputy Head of the Department.

Dan Rujescu is mostly involved in the research of genetic factors and biomarkers of psychiatric diseases. The Department is involved in extensive academic and industrial national and international genome and post-genome efforts (e.g. genome wide association studies, next generation sequencing etc.). The major focus of his research is on a multidimensional translational approach to neuropsychiatric diseases and behavioral phenotypes at genetic, molecular, cellular, structural, functional, cognitive and behavioural levels integrating animal models. The group is recruiting and characterizing one of the largest groups of psychiatric patients and controls with intermediate phenotypes.

This talk will give an overview on the current stage of genomics in psychiatric diseases and show examples for successful identification of new genetic components and pathways. Furthermore, examples for systems biology approaches will be given.

Dr. Henriette Uhlenhaut, HMGU

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Dr. Henriette Uhlenhaut obtained her "Diplom" in Biotechnology in 2002 from the Technical University in Braunschweig. She also holds a Master of Science degree in Applied Biology from the Georgia Institute of Technology in Atlanta, GA, USA (2000). Dr. Uhlenhaut earned her PhD in Molecular Biology from the EMBL University of Heidelberg Joint PhD Program (2007). She then went on for postdoctoral training at the Salk Institute for Biological Studies in San Diego, California, and at the Max Delbrück Center for Molecular Medicine in Berlin. Since 2013 she is heading the independent Emmy Noether Research Group "Molecular Endocrinology" at the Helmholtz Zentrum München.

From very early on during her career, Dr. Uhlenhaut started applying genomic approaches towards understanding the genetic mechanisms underlying physiology and development. She first used microarrays to determine the impact of natural variation on flowering time in *Arabidopsis thaliana*, and then continued to perform expression profiling and data analyses in mouse models for human disease. She has been especially interested in discovering novel ways of transcriptional repression, which has led her towards nuclear hormone receptors. Her lab uses a combination of cutting edge genomics, mainly using NGS technology, to study gene regulation by nuclear receptors.

Dr. Desislava Boyanova, HMGU

Dr. Boyanova obtained her Master of Science degree in 2009 after studying Biomedicine at the University of Würzburg. Then she continued her academic path in Würzburg with a PhD thesis in the field of Bioinformatics (2012). Since 2013 she is a Postdoc at the Institute for Bioinformatics (IBIS) at the Helmholtz Center.

Before joining Helmholtz Center, Dr. Boyanova analyzed proteomics data in human platelets. She also worked on the development and optimization of network search algorithms and functional module analysis. At Helmholtz she entered the field of genetics and genetic variation of nuclear receptors and their targets. She investigates the impact of common SNPs in nuclear receptor targets on human phenotypes such as metabolomics and gene expression. She is also involved in projects on Chip-Seq and RNA-seq data from Dr. Uhlenhaut's lab.

Nuclear receptor genomics

Our genome consists of roughly three billion basepairs, but coding sequences make up only a small percentage. From the ENCODE project and other studies, we now know that intergenic DNA sequences contain far more regulatory regions than previously thought, and that large parts of the genome are anything but "junk DNA". Using genomic and bioinformatics technologies, we are beginning to unravel the complex regulatory features contained in enhancers and other elements, to understand the combinatorial codes and the intricate logic that are encoded in these sequences, and that are required for tissue- and signal-specific transcriptional responses. Genetic changes in these regulatory regions could have an impact on the expression and functionality of regulated genes.

Nuclear hormone receptors comprise a large family of ligand-gated transcription factors that act as important regulators of numerous physiological processes such as reproduction, metabolism, homeostasis, inflammation and development. To regulate gene expression, nuclear receptors bind to consensus DNA sequences known as hormone response elements.

Dr. Uhlenhaut studies the interaction of nuclear receptors (with a focus on the glucocorticoid receptor) with the chromatin landscape and the assembly of transcriptional complexes using ChIP-Seq analysis coupled with RNA-Seq. Dr. Boyanova combines knowledge on genetic variance of nuclear receptors with SNP correlations to metabolic phenotypes. SNPs can have a functional impact on DNA splicing, protein truncation, DNA regulation, metabolite concentrations and disease.
By combining efforts in analyzing expression quantitative trait loci (eQTLs) in GR binding sites we investigate the role of non-coding genetic loci correlating with gene expression. Bioinformatic hypotheses based on the genomic location of SNPs in GR binding sites can then be further tested in the wet lab.

We will give an overview of how next generation sequencing studies and bioinformatic data analyses go hand in hand to elucidate nuclear receptor function.

Prof. Dr. Thomas Werner, Univ. of Michigan, Ann Arbor

Adjunct Professor for Internal Medicine-Nephrology Division at the University of Michigan, Ann Arbor, USA. Educated as a chemist at the LMU Munich he completed his PhD in Biochemistry at the same University (1986) and "habilitated" at the TU Munich in the fields of Genetics (2003). He founded a bioinformatics group at the Helmholtz-Zentrum (formerly known as GSF) in 1988 focusing of gene regulation, especially promoter analysis, and founded Genomatix Software GmbH in 1997, where he served as CEO & CSO until 2009. He is now a member of the Board of Genomatix and works as an independent Scientific & Business consultant.

Main interest: gene regulation, comparative genomics, pattern recognition, next generation sequencing, network analysis, translational omics-based precision medicine.

Translational Transcriptomics: We have learned from the ENCODE project and a large body of recent literature that disease-relevant gene regulation is tightly integrated including genomic mutations, epigenetic remodeling, transcription, post-transcriptional regulation and translation and post-translational control. Not all aspects are easily assessed in routine analysis but the availability of microarrays and increasingly also NGS-methods such as DNA-genotyping and RNA-seq analyses have opened new opportunities to apply omics-based methods in order to gain medically relevant insights. However, there is still a large gap between even the most sophisticated statistical methods, their results, and the biomedical functional information clinicians will require to finally be able to base their diagnosis and therapeutic decisions on such omics-data analyses results. Precision medicine necessarily needs to look at the whole system (old-fashioned called "patient") while omics methods are limited to analyses of particular aspects of the system only. A molecular modeling of a complete human is impossible and probably also not required. As a result we must simplify our approaches either way: Limiting to a sub-system but faithfully following nature in terms of complexity, or trying to gain a broader overview necessitating compromises on the biological details. Both approaches have been taken and both have their own advantages and perils.

I will focus on an overview of how the requirements of precision medicine (both in diagnostics as well as in therapeutics) change the demands on a high-through data analysis pipelines for transcriptomics data. Analysis goals and paradigms have to be changed from the viewpoint of application in translational medicine. We shall discuss how this changes the viewpoint from the bioinformatics side, in terms of data and analysis results, and as a consequence also education. .