16th Spring School Bioinformatics Bertinoro, Italy

HELENA
Helmholtz Graduate School Environmental Health

The 16th edition of the Spring School of Bioinformatics will be held from 12st through 16th March 2016. 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 open to other Ph.D. students and post-graduates.

Lecturers and Topics

Lecturer	Affiliation	Topic
B. Brors	DKFZ Heidelberg	Cancer Genomics - what can we learn from massive sequencing tumor samples?
M. Campillos	Helmholtz Zentrum München (HMGU)	Systems Pharmacology
C. Eckerskorn	Biomax Informatics AG, Planegg	Knowledge Models and Data Integration
L.J. Jensen	Univ. Kopenhagen, Panum Inst.	Large-scale integration of data and text for medicine
G. Kastenmüller	HMGU, IBIS	Metabolomics for Personalized Medicine
J. Krumsiek	HMGU, CMB	Systems Biology and Models
R. Küffner	HMGU	NGS pipelines and technical infrastructure
H.W. Mewes	Technische Univ. München & HMGU	Causality, Systems Biology, Big Data and Individualized Medicine
A. Pfeufer	HMGU, IBIS	Large-scale Data in Human Genetics
H. Prokisch	HMGU, TUM	Genetics of rare mitochondrial diseases
T. Rattei	Univ. Vienna	Microbiomes in health and disease
T. Werner	Univ. of Michigan, Ann Arbor	Association and Relevance - Opportunities and Limitations in Translational Transcriptomics

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

Outline of the Course

Accumulated data is superior to any individual knowledge, but much less understood. Our society is controlled by information driven technologies mastering exchange, storage and analysis of data. Digital data collection and communication technologies are play a central role in the ongoing intellectual and economic evolution. We need fresh concepts to move from written notes and publications on paper to the power of data driven research. We now have instant access to more information than any individual can ever digest.

Social and financial networks, as well as information flow in every moment of our daily live become essential, not always for the better. The information space will became a firm part of the life sciences as well. Medical applications will benefit from biological knowledge. How to deal with information needs to be included in training and education of young scientists. The goal to reduce multi-dimensional data to simple comprehensible rules is a far-reaching one. For the practical need to transform data into knowledge and turn knowledge into advice for therapies, we need to learn how to master information and communication technologies (ICT).

The reality of life science research aims for the exploration of the enormous power of data and the need to support clear-cut solutions to serve the pressing needs of an ageing society in the industrial countries on the one hand and the bare necessity to cope with the basic needs of a fast growing global population on the other.

This year's course aims for an introduction to the challenges and promises of foundations (bioinformatics), paradigms (systems biology), and applications ("Big Data") in the life sciences. Given the data, we must be able to select the best therapy for the individual patient, the goal of **personalized medicine**. How to interpret data from the gut microbiome relevant for metabolic disorders? For complex diseases such as diabetes or schizophrenia, we need to identify causes and optimize antipsychotic treatment. There is a need for collaboration between experimentalists and bioinformaticians to collaborate on complex problems and large scale systematic programmes. What are the suitable concepts to tackle complex biology and genetics? What are the research areas that contribute to the translation of basic research into the clinic? These topics will be addressed in the course lectures.

Even a simple biological system such as a prokaryotic cell consists of thousands of variables describing the cellular information. Multicellular organisms are far more complex; 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 their interpretation in context of any related biological knowledge.

Big Data and Personalized Medicine stands for paradigms that are far from being well defined. At least, it aims for a structured approach to distinguish the (disease) state from one individual to another. Take another twist of massive data integration: can we employ sequence and phenotype data at large? Obviously we need to implement computational methods that enable

us to apply lessons learned from Big Data to the life sciences.

Bioinformatics and Computational Biology has developed 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 experimentalist and the bioinformatician: 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 magic black box that instantly returns something "ready for publication" after the experiment has generated complex data.

The Spring School gears for the understanding of concepts and how these can be applied in practice. What is the role of algorithms, data, and biological knowledge? We will discuss why we need network analysis and what are the methods required to organize and interpret data.

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/HMGU in the morning of March 12th.

Course Schedule and additional information:

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

DIRECTOR:

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

Bioinformatics Spring School
12.03. – 16.03. 2016

Saturday, 12. 03. 2016
Arrival Bertinoro

Sunday, 13. 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	C. Eckerskorn	Smart Data: Objectives and vision of precision medicine
15:30 – 17:00	L.J. Jensen	Gene Association Networks: Large-scale integration of data and text

Monday, 14. 03.

8:30 – 10:30	T. Werner	Translational Transcriptomics: Opportunities and Limitations
11:00 – 12:30	G. Kastenmüller	Metabolomics for individual genetics
13:30 – 15:00	J. Krumsiek	Quantitative models and simulation for Systems Biology
15:15 – 16:45	H.W. Mewes	Big Data, Causality, and Personalized Medicine

Tuesday, 15. 03.

9:00 – 10:30	A. Pfeufer	Large scale data in genetics - From association to causality
11:00 – 12:30	R. Küffner	Regulatory Networks
13:30 – 15:00	M. Campillos	Systems Pharmacology
15:30 – 17:00	B. Brors	Cancer Genomics

Wednesday, 16. 03.

09:00 - 11:00	H. Prokisch	Mitochondrial Diseases
11:15 - 12:00	R. Küffner	Final Roundtable
13:00	Departure	Bus to Munich

Faculty members and abstracts
16th Course on Bioinformatics and Systems Biology

Prof. Benedikt Brors
DKFZ Heidelberg

Benedikt Brors studied chemistry in Düsseldorf and graduated in biochemistry there. He then joined the German Cancer Research Center in Heidelberg as a postdoctoral fellow in the Division of Theoretical Bioinformatics. In 2003, he became head of a research group in Computational Oncology, where he developed algorithms to analyse high-dimensional data from a number of different omics technologies. In 2014, he was appointed to a post as as full professor and head of the newly established Division of Applied Bioinformatics at DKFZ, where his main interest is in clinical application of bioinformatic data analysis, most prominently in the precision oncology program of the National Center of Tumor Diseases in Heidelberg, where he is a co-affiliate. He is PI in a number of national and international initiatives within the International Cancer Genome Consortium, the International Human Epigenome Consortium, the CancerSys, e:bio and e:med initiatives, as well as a coordinator of the sequencing platform in the German Cancer Consortium.

Cancer genomics studies the somatic alterations in cancer cells on a broad scale by employing high-volume technologies such as whole-genome or whole-exome sequencing, transcriptomic profiling, or epigenome analysis. By comparing malignant and normal cells from the same patients, aberrations that are due to the cancerogenic process become evident. This allows to identify driver events, study tumor evolution and heterogeneity in detail as well as derive hypotheses on mutation-generating mechanisms. The data can also be used to stratify patients to targeted treatments based on their molecular alterations, or to guide immune therapy approaches. In my talk, I will highlight recent findings on selected cancer entities and discuss the implications for future strategies towards a personlized treatment in cancer care.

Dr. Monica Campillos,
Helmholtz Zentrum München

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

Systems Pharmacology

Systems Pharmacology applies systems biology principles to the field of pharmacology in order to understand and predict the effect of drugs in the human organism. To that aim, systems pharmacology deals with the analysis and integration of large-scale databases containing medical and biological information of drugs. In this talk, I will give an overview of the evolution of Systems Pharmacology field, from its origin to its recent contribution to advance personalize medicine and drug combination treatments. I will talk about seminal research studies analyzing the human druggable genome and elucidating properties of drug-target and drug-diseases networks, discuss computational methods to infer drug targets and highlight recent systems pharmacology approaches towards developing personalized treatments and effective drug combinations.

PD Dr. Christoph Eckerskorn
Biomax Informatics AG

Christoph Eckerskorn is currently working at Biomax Informatics AG (Corporate Business Development) and is partner of the Munich Inter Consulting AG (MIC). With more than 20 years of professional experience (of which 10 years in research), he has been responsible for research and development of new technologies and methods and their related commercialization in newly created Life Sciences business sectors. A special focus involved the identification, characterization, and validation of biomarkers as well as the development and automation of the related processes.

He studied Chemistry in Munich before advancing to the Max Plank Institute for Biochemistry where he obtained his doctorate in protein analysis and virology. After his postdoctoral work at the University of Michigan, Department of Pediatrics, Ann Arbor, and at the University of Münster (Habilitation and Venia Legendi in Analytical Biochemistry), he managed the Service Department for Mass Spectronomy at the Max Plank Institute for Biochemistry.

His extensive career experience in the Life Sciences industry has spanned management of a start-up company specialized in commercial bioanalytics to leading positions in general management, operational business, research and development, business development, and strategy conceptualization for new business thrusts for a well-known, global enterprise focused on laboratory automation, diagnostics, test development, pre-clinics and production of equipment. These leading positions have included General Manager, Chief Science Officer, and Vice-President of Research and Development.

Smart Data: Objectives and vision of precision medicine
Precision Medicine refers to the tailoring of medical treatment to the individual characteristics of each patient. It does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not. Although the term ‘Personalized Medicine’ is also used to convey this meaning, that term is sometimes misinterpreted as implying that unique treatments can be designed for each individual.

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 where 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 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 founder, owner and scientific advisor of Intomics A/S. He is a co-author of more than 150 scientific publications that have in total received more than 15,000 citations. He was awarded the Lundbeck Foundation Talent Prize in 2003, his work on cell-cycle research was named "Break-through of the Year" in 2006 by the magazine Ingeniøren, his work on text mining won the first prize in the "Elsevier Grand Challenge: Knowledge Enhancement in the Life Sciences" in 2009, and he was awarded the Lundbeck Foundation Prize for Young Scientists in 2010.

Gene association networks: **Large-scale integration of data and text**
Methodological advances have in recent years given us unprecedented information on the molecular details of living cells. However, it remains a challenge to collect all the available data on individual genes and to integrate the highly heterogeneous evidence available with what is described in the scientific literature.

In my presentation I will describe the STRING database (http://string-db.org), which is widely used in the proteomics community. It aims to provide critical assessment and comprehensive integration of protein–protein interactions, including both direct physical interactions and indirect functional associations. The latest version of STRING covers more than 2000 organisms for which it includes evidence from a diverse range of curated databases, raw data repositories, automatic text mining of biomedical literature, and computational prediction methods. I will also briefly introduce a suite of web resources that apply the same strategy to study subcellular localization (http://compartments.jensenlab.org), tissue expression (http://tissues.jensenlab.org), and disease associations (http://diseases.jensenlab.org).

Dr. Gabi Kastenmüller
Helmholtz Zentrum München

Dr. Kastenmüller heads the research group “Metabolomics” at the Institute of Bioinformatics and Systems Biology (IBIS), Helmholtz Zentrum München, and is an Honorary Lecturer in the Department of Twin Research, King's College London, UK. Holding master's degrees in chemistry and computer science, she moved into bioinformatics for her PhD, which she obtained from the Technische Universität München in 2009 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 at IBIS, 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, which mainly focuses on the analysis and interpretation of high-throughput metabolomics data sets from clinical as well as epidemiological projects. In particular, the group is interested in the inborn metabolic individuality in human populations and how this individuality affects predisposition to diseases and response to treatments.

Metabolomics – a tool for personalized medicine
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 investigates the end point of all regulatory and enzymatic processes in the system, which is influenced by genetic and environmental factors. Metabolomic profiles of biological samples such as blood or urine samples are thus considered to represent snapshots of the donors’ current physiological states. Confirming this assumption, strong associations of specific metabolomic profiles with a variety of diseases have been identified in recent years. Recording individual profiles over time using high-throughput metabolomics in a clinical setting might open new avenues to detect and prevent diseases in an early stage and could be used to better monitor individual response to treatment in precision medicine. Efficient processing of growing clinical metabolomics data sets and their combination with and interpretation in the context of other clinical and omics parameters will be key for the success of clinical metabolomics.

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 a short overview of all steps in the analysis of data produced by these approaches. Finally, I will present selected examples of current metabolomics projects, discussing strengths of the metabolomics approach as well as challenges in data analysis and interpretation.

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, between 2003 and 2014, working 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 Next Generation Sequencing (NGS) 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.

An infrastructure for professional NGS data analysis

One of the great current challenges in biomedical research is to provide the bioinformatics necessary for the utilization of Big Data. Experimental labs need optimal support in the analysis and interpretation of big data towards the functional validation of disease factors and biomarkers. The unique challenges associated with Big Data in general are characterized by their sheer volume and complexity. To address these challenges efficiently, we create solutions for storage: to ensure security, availability and fast access to Big Data sets, data processing: via efficient, reproducible and maintainable workflows and knowledge integration: interpretation of results using third party databases. Required resources for development and maintenance as well as technical difficulties are easy to be underestimated. Instead of a from-scratch approach, we integrate professional, available and fully developed tools with intuitive interfaces useful to both experimentalists and bioinformaticians. Within this infrastructure, my next generation sequencing (NGS) group at the Helmholtz center built up strategic competence across all important NGS areas. NGS has become a key technology in life science for diagnosis, treatment and comprehension of human diseases. NGS benefits from technological breakthroughs and its unequaled versatility -- based on one technology, we detect gene and genome variations as well as epigenetic modifications and changes in methylation, messenger RNA and ncRNA expression levels. With millions of organism- wide datasets, the real challenge is the interpretation of the complex NGS results. Here, we perform comprehensive statistical analysis of NGS data to discover disease relevant genes and variants in various projects involving e.g. tumor genomes, pharmacogenomics and schizophrenia patients.

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. From 2013-2016, he lead a research team on 'Systems Metabolomics' at the Institute of Computational Biology, Helmholtz Zentrum München, and worked as a visiting fellow at the Weill Cornell Medical College, New York City, USA. Starting early 2016, he heads a Helmholtz Young Investigator Group called 'Systems Medicine of Diabetes'.

Quantitative models and Systems Medicine

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. A recent branch of Systems Biology is Systems Medicine, which focusses on human data, disease phenotypes and the translation to clinical practice.

In this talk we will go through basic principles of mathematical modeling and biostatistics, covering differential equations, mass-action kinetics, enzyme-catalyzed reactions, stability analysis, discrete modeling approaches, network biology and machine learning. We will discuss all methods in the context of real biological examples like, for example, stem cell differentiation mechanisms and metabolomics measurements. Moreover, we will discuss if and how results from such studies can be transferred to actual clinical applications

Prof. 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 and Big Data:

Access to our own blueprint in its most personal form, the own genome is soon becoming routine. The power to compare all of your 3 billion bases to other billions of genomes becomes not only feasible, even the mapping to the personal phenotype and its course from birth to death will be somewhere in the data space. Will genetic determination or even the increased odds for disease chance our lives from faith to prediction? Obviously the answer to this question will have heavy consequences for our hopes and fears as much as the chances for the prevention of otherwise unavoidable consequences of our genetic make-up.

At present, 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. Our belief that the data lead us to a clear understanding of mechanisms involved is build on mechanistic model of the world, based on cause and effect. But the gene/environment concept that shapes our health state, involves thousands of variables generated by genetic variance, ageing, and everything 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 and the impact of massive data to come.

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.

"Large scale data in genetics - From association to causality"

Genetic predisposition to disease comprises both high effect low allele frequency genome variants (i.e. rare mutations in monogenic diseases, rare disease rare variants, RDRV) as well as low effect high allele frequency genome variants (i.e. common predisposing polymorphisms, common disease common variants, CDCV). 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. Using Second generation sequencing technology and genotyping arrays both types of genome variants are now accessible at a reasonable cost. My presentation will focus current bioinformatic, human genetic and genetic epidemiology concepts with respect to genetic disease risk and predisposition. I will especially focus on how in current research large sets of patients are necessary for both CDCV and RDRV research, how they are generated, handled and what the concepts, issues and limitations of their scientific study are today.

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. Thomas Werner
Univ. of Michigan, Ann Arbor //OK//

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.

Association and Relevance - Opportunities and Limitations in Translational Transcriptomics

NGS-based whole transcriptomes have almost become a routine and will be introduced into the clinical practice in the not too far future. However, transcriptome data are essentially this - data, not knowledge upon which any diagnostic or therapeutic decision can be directly based. For this purpose interpretation of the data is required to provide higher-level knowledge that will allow medical interpretation. We have an impressive array of computational tools allowing us to locate significant differences between disease and normal states as well as to associate these changes with biological processes, pathways, and diseases. The crux remains that "significant" by no means guarantees that such differences are also relevant and an association, regardless how low the p-value drops, does not imply causality. Unfortunately, relevance and causality is exactly what medical decisions in personalized medicine need to be based on. On top of that medical decisions necessarily needs to look at the whole system (old-fashioned called "patient") while transcriptomics is limited to particulars aspect of the system or even part of the system (e.g. blood cells). This does not necessitate molecular modeling of a complete human but does require a simplifation of 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. However, dealing with the significance/relevance and association/causality problem is common to all approaches. I will use an example of GWAS / eQTL analysis to show where those conflicts arise along the analysis and what has been tried to overcome them.