



Horizon Breakthrough Projects

Granted Projects- Sixth Call

Dissecting the splicing process of the 2.4 Mb DMD gene by deep sequencing

Dr. A. (Annemieke) Aartsma-Rus (v), 12-09-1977, Leiden, LUMC – Humane Genetica
Splicing is a complex process, that takes place in all our cells, in which a gene is converted into a protein code. This process is especially complex for the dystrophin gene, as this is the largest human gene. The researchers will study dystrophin splicing in more detail in order to optimize a therapy that modulates splicing (“exon skipping”).

Exosome signaling in vascular endothelial repair: elucidating the mechanism of RNA sorting to exosomes

Dr B.W.M. (Bas) van Balkom (m) 01-07-1974, Breda, UMC Utrecht – Experimental Nephrology
Cells can communicate with each other over long distances. They have developed an ingenious way to pack carefully selected, complex information into small vesicles. The researchers will investigate how messages are selected for packaging into vesicles, and why this sometimes fails, for example during stress or disease.

An innovative approach to identify new epitopes in hepatitis C virus for generation of novel dendritic cell-based vaccines

Dr. M. (Marianne) Boes (v) 26-03-1973, Wormerveer, UMC-Utrecht – Pediatric Immunology
Hepatitis C virus infections are the underlying cause of the majority of liver cancer cases, and necessity for liver transplantation. The development of successful vaccines that prevent infection has not yet been successful using existing techniques. This project tests a new method to develop new vaccines to prevent hepatitis C virus infection resulting in chronic hepatitis.

Delve deeper into proteomes: A targeted de novo sequencing algorithm allows efficient protein identification with mass spectrometry

Dr. Ir. B. (Bas) van Breukelen (m) Arnhem, march 24 1974. Utrecht University, Biomolecular Mass Spectrometry and Proteomics group
Proteomics techniques enable large scale identification of proteins. Good and bad proteins are recognized as a kind of barcode and via comparison to known databases. This is impossible when these proteins are not in such databases. In this research a method will be developed that will allow the identification of those proteins.

Deconvolution of plant phenolic metabolism using multidimensional metabolomics

Dr Y.H. (Young) Choi (m) 08-05-1968, Seoul (South Korea), LU - Pharmacognosy
Plants produce defence compounds upon the attack of diverse organisms. The researchers will analyze the role of different parts of a cell in the production of all compounds involved in the defence through time.

When Kingdoms collide: genome-wide responses to co-cultivation of pro- and eukaryotes

Dr. Ir. P. (Pascale) Daran-Lapujade (f) 05-04-1972, Toulouse, Delft University of Technology - Industrial Microbiology

Yeast and lactic acid bacteria co-exist in natural environments (e.g. Oral cavity) and in food and beverage fermentations (e.g. cheese, beer). This research will explore the nature of this collaboration, aiming at improving industrial processes and personal care (oral hygiene).



Combining ChIP-seq data with gene expression and protein structure: towards understanding specificity of DNA recognition by plant MADS transcription factors

Dr. A.D.J. (Aalt-Jan) van Dijk (m) 7-10-1979, Utrecht, Wageningen UR, PRI ,
Applied Bioinformatics

Plant MADS proteins regulate many developmental processes such as the transition to flowering. In order to do so, they bind to DNA, and although all MADS proteins are very similar, they recognize different DNA sequences. The project will combine experimental data with bioinformatics, leading to an understanding of this recognition process. This will have important applications in plant breeding and biotechnology.

A Chemical Genomics Screen to Identify Suppressors and Enhancers of Cell Competence for Regeneration

Dr. M.A. (Martijn) Fiers (m) 9-3-1972, Bladel, WUR- Plant Sciences Group

In the life cycle of plants embryos are formed after fertilisation which in time will develop into a new generation of plants. The researchers will search for chemicals which can induce the formation of embryos on the plant without fertilisation and in such a way discovering new insights in embryo induction.

Identifying causative copy number variants in immune related disorders

Dr. L. (Lude) Franke (m) 14-01-1980, Oldenzaal, UMCG – Genetics

Recently it has become evident that people can live healthy while they miss considerable amounts of DNA. However, if different parts of their DNA miss they suddenly get ill. This project will investigate the role of absent DNA in immune-related disorders, such as rheumatoid arthritis; type 1 diabetes and coeliac disease will be investigated.

The two sides of RelB in immunity unraveled: a genome-wide search for the role of chromatin

Dr. S.I. (Sonja) Gringhuis (v) 09-11-1969, Stadskanaal, VUmc – Molecular Cell
biology & Immunology

Our body responds to ill-making microbes by producing proteins that instruct the cells of the immune system to act against the invaders. The production of proteins is regulated by factors that function as 'on/off switches'. The researchers will analyse why one such a switch turns the production of some proteins 'on', while simultaneously turning 'off' the production of other proteins. This research is important to combat infections.

High-resolution analysis of point and structural genome variants and their effect
on gene expression

Dr V. (Victor) Guryev (m) 31-08-1976, Tasjkent (Sov. Unie), Hubrecht Institute,
UMC - Genome Biology

Your genome is very different from mine. This difference defines our appearances, but also our diseases. The researchers will compare genomes of rats with high and normal blood pressures to find genes that play role in this common disease.

Role of alternative splicing in plants' adaptation to a changing environment

Dr. Ir. R.G.H. (Richard) Immink (m) 13-03-1973, Ommen, Wageningen University – Plant
Sciences Group

Global warming influences flowering time of plants and as a consequence some species spread outside their native region. Flowering is essential for plant existence. In this projects scientists will decipher how plants are able to cope with changes in ambient temperatures.



Dissecting the epigenetic architecture of complex traits

Dr (Frank) Johannes (m) 01-02-1976, Dresden (Germany), University of Groningen – Groningen Bioinformatics Centre

For good or for bad, children tend to resemble their parents. Researchers will show that neither shared environment nor DNA are the only reasons for this, but that epigenetic ""marks"" on the DNA allow for soft-coded and environment-sensitive inheritance.

Silencing resistance: crop protection via in planta expression of dsRNAs targeting herbivore mRNAs

Dr. M. R. (Merijn) Kant (m), 22-07-1969, Amsterdam, UvA - Population Biology (Institute for Biodiversity and Ecosystem Dynamics)

In this project the investigators will work on developing a novel method for protecting crops against pests, based on RNA interference (RNAi). RNAi is a process that blocks gene expression. They hope to show that RNAi can be used to limit feeding damage on tomato plants caused by a ravenous pest organism, the two-spotted spider mite. To do so they will modify tomatoes in such a way that, after the mites have ingested the content of plant cells, it will interfere with the expression of mite genes essential for their survival. If successful this project will open the way for applying functional genomics in targeted pest control.

Genome-wide assessment of Cis-regulatory evolution and morphological innovation in flower & fruit development

Dr. K. (Kerstin) Kaufmann (f) 19-07-1977, Salzwedel, Germany. Wageningen University, Molecular Biology

Flowers and fruits come in a variety of forms and sizes. This diversity is even obvious among closely related plant species. How this variation evolved and which genes played a role in this process, is still a mystery for scientists. One hypothesis is that proteins which regulate the expression of genes work differently comparing different plant species, resulting in the evolution of morphological diversity.

Genomics-based cell engineering for improved uptake of hydrophobic substrates in whole-cell biocatalysis

Dr A. (Anett) Kirschner (f) 04-05-1981, Grossenhain (Germany), RUG – Biochemistry
Bacteria can be used as bioreactors to perform chemical reactions. Often, uptake of chemicals into industrially relevant bacterial cells is inefficient. Therefore, the researchers want to explore nature's diversity for new transport proteins that improve uptake of these chemicals.

Yeast based valorization of plant metabolic diversity: Engineering *Saccharomyces cerevisiae* for the production of anthocyanin antioxidants

Dr. ir. A.J.A. (Ton) van Maris (m) 31-05-1976, Haarlem, Delft University of Technology - Industrial Microbiology

Plants are full of many healthy compounds, including the well known colour compounds of blueberries and grapes. By making these so called antioxidants in baker's yeast it will be easier to see how the individual compounds influence human health.

Ubiquitinated Peptide Selection (UPS); Isolation of gly-gly modified peptides to identify UV induced differences in ubiquitination

Dr. Ir. J.A.F. (Jurgen) Marteiijn, (m) 05-02-1977, Oostburg ErasmusMC, Genetics

Our DNA is continuously damaged, if this damage is not correctly repaired this can result in the onset of cancer or accelerated aging. In this project we will investigate how the activity of DNA repair proteins is regulated. Using a proteomics approach we will identify which proteins are regulated by ubiquitination after UV-induced DNA damage.



Multiplex Imaging of Tissue Arrays

Dr. L.A. (Liam) McDonnell (M), 4-6-1975 (United Kingdom), LUMC, Department of Parasitology, Biomolecular Mass Spectrometry Unit

Current techniques used for pathological research, and patient diagnosis/prognosis supply a large amount of data. The researchers will develop data reduction strategies. The developed tool can be applied to pathological examination of soft tissue tumours, cancers in which differential diagnosis can be very challenging.

Comprehensive analysis of RNA species in immune cell exosomes and their effects on the transcriptome of target cells

Dr E.N.M. (Esther) Nolte-'t Hoen (f) 08-07-1976, Hilversum, UU – Veterinary Medicine, Biochemistry and Cell Biology

Communication between immune cells is crucial to establish immune responses. A rather unexplored way of intercellular communication is via secreted vesicles. Immune cells can produce small vesicles containing proteins and genetic material to send information to neighboring cells. The researcher will decode the genetic messages transferred via these vesicles.

Systems-level exposure of the role of latent metabolism in evolutionary adaptation

Dr R.A. (Richard) Notebaart (m) 16-10-1980, Rotterdam, Radboud Universiteit Nijmegen - Bioinformatica

Bacteria are able to convert nutrients from the environment into components of which the bacteria is built up from. This is called metabolism and it allows the bacteria to grow and reproduce.

The researchers will expose hidden parts of metabolism which contribute to growth.

Genomic selection analysis as a tool for unraveling the genetic basis of life-history traits

Dr. B.A. (Bart) Pannebakker (m) 18-06-1976, Leiderdorp, RuG – Evolutionary Genetics

For any organism, development, survival and reproduction are important traits which together define its life-history. As Darwin proposed, evolution fine-tunes life-histories to optimally match an organisms environment by selecting heritable adaptations. This research will apply new methods to determine how such adaptations are encoded in the genetic material of a parasitic wasp.

Identification of new malaria invasion proteins as putative targets for drug and vaccine development

Dr. E.M. (Erica) Pasini (v) 09-01-1974, Milan, Italy, BPRC – Parasitology

For success in controlling malaria parasites a vaccine and new drugs are urgently needed.

Proteins at the parasite surface are exposed and potentially vulnerable to vaccines and drugs.

This project will determine the vaccine and drug potential for 10 malaria surface proteins recently identified by the research group.

MicroRNAs, novel targets to repair cerebrovascular function and restore brain homeostasis in neurological disease

Dr. ir. A. (Arie) Reijerkerk (m) 14-09-1974, Haarlemmermeer, VUmc - Moleculaire Celbiologie en Immunologie

Recently discovered small RNA molecules called microRNAs regulate numerous important processes in our bodies. It is becoming more and more clear that these tiny regulators are also in charge of finetuning brain blood vessel function. Blood vessels in the brain are uniquely equipped to ensure normal functioning but are disturbed in multiple sclerosis patients. The researchers will investigate the status of miRNAs in brain vessels of patients with multiple sclerosis.

The small RNAome of mosquito-transmitted viruses

Dr. ir. R.P. (Ronald) van Rij (m) 17-09-1972, Hellevoetsluis, UMC St Radboud - Medical Microbiology

Vertebrates have a complex system for the defence against disease makers like viruses. Mosquitoes do without this immune system, and use another defence mechanism: RNA interference. With this mechanism the mosquito degrades the genetic material (RNA) of a virus into small debris. The researchers will study these small RNAs from viruses that are spread by mosquitoes, like the Dengue virus.

MicroRNAs as hallmarks of susceptibility to viral heart disease

Dr. B. (Blanche) Schroen (v) 30-06-1980, Maastricht, UM - Center for Heart Failure Research
In young people a viral infection of the heart can result in heart failure. However, not everyone is susceptible. The researcher will search for new risk-genes in heart and blood in order to explain the susceptibility of the heart.

Unlocking the genome of intracellular marine sponge symbionts: novel insight in evolution and biotechnological potential of hidden microbes

Dr D. (Detmer) Sipkema (m) 20-08-1975 (Groningen), Rhenen, WUR - Microbiology
Marine sponges are the oldest multicellular organisms on earth. Most sponges are associated with complex communities of microorganisms that are often also producers of many secondary metabolites of interest for pharmaceutical applications. This project aims at elucidating the genome of the intracellular microbial symbiont of the sponge *Crambe crambe*. This can help us to understand the early evolution of symbiosis, and to elucidate the close relationships between the sponge and its microbial partner.

miRNA regulation of coagulation and thrombosis

Dr C.Y. (Carla) Vossen (v) 27-04-1976, Gouda, LUMC-Clinical Epidemiology
Abnormal clotting of the blood (thrombosis) is common and can have major consequences. Recently, it was found that small pieces of genetic material, microRNAs, can influence the levels of many proteins. The researchers will study the role of microRNAs in normal blood clotting and thrombosis.

Dissecting sequential substrate utilization in *Aspergillus niger* using transcriptomics and proteomics

Dr. Ir. R.P. (Ronald) de Vries (m) 15-10-1967, Wageningen, UU - Microbiology
Fungi use food sources in a specific order, by degrading these sequentially with enzymes. The researchers will determine how this is organized for the fungus *Aspergillus niger* by analyzing which enzymes are produced, and in which sequence they are produced.

Computational Framework for Dynamic ¹³C Labeling Experiments in Micro-organisms for in-vivo Kinetic Modeling

Dr. Ir. S.A. (Aljoscha) Wahl (m) 01-06-1976, Stuttgart (Germany), Delft University of Technology – Biotechnology
Microbial metabolism is regulated by different mechanisms. To understand the metabolic interactions enzyme kinetics are needed. Bioengineers will analyze the kinetics of metabolism in living cells using specialized techniques (¹³C tracers).

A new concept for the pathogenesis of psoriasis: Lessons from genetics and functional genomics

Dr. P.L.J.M. (Patrick) Zeeuwen (m) 15-07-1966, Zoetermeer, RUNMC – Dermatology
The most important genetic risk factors of the skin disease psoriasis are clear. Now, researcher focus again more on the cell biological mechanisms. With the aid of reconstructed skin as a model system, the role of the skin barrier and the interaction with micro organisms are mapped.