EADGENE

Success Stories

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EADGENE' Achievements over the last 5 Years

Marie-Hélène Pinard-van der Laan, INRA, France

It is with great pride, but also with a hint of "nostalgie", that I present to you this EADGENE successes brochure.

Great pride for all that has been accomplished thanks to the hard work, commitment and, above all, faith in this adventure that was called the "Network of Excellence (NoE)". Five years ago, many were sceptical about NoE: What was the meaning of integration? Could you really carry out research in a NoE? Fortunately, some of us were enthusiastic enough about this idea to get it started. Gradually, ongoing collaborations have been strengthened, new collaborations have been facilitated, exchanges of people and resources have been taking place, people have got to know each other and we have had the pleasure of meeting at our workshops, partner meetings, yearly EADGENE days... and a real Network arose!

The "Success Stories" presented in this brochure provide true evidence of the significant outputs and impacts of the EADGENE NoE; which would not have happened otherwise... and many additional successes we didn't even think about when we started!

You may be amazed by the diversity and the quality of achievements. You will read about integrating resources, developing and sharing up-to-date technologies and tools, successful collaborative research outputs on host-pathogen interactions in several models, bridging the gaps between research and industry, increasing exchanges of ideas and knowledge through mobility, workshops and meetings, while challenging ourselves with ethical concerns.

Of course I am a little bit nostalgic as these 5 years have passed. However, we will continue as a "European Research Group", an informal grouping of our institutions, and fortunately with the EADGENE_S project (2-year ECCSA project, 2011-2012). Activities will also continue through joined projects in which many of our partners participate, e.g. the NADIR (Network for animal diseases/infectiology research infrastructures initiative with 15 partners from within and outside EADGENE http://www.nadir-project.eu/nadir_project).

The Virtual Lab: Sharing Resources and Facilities

Ingrid Olsaker, Norwegian School of Veterinary Science, Norway

One of the primary objectives of the EADGENE Network is to coordinate and facilitate access and sharing of biological resources and advanced technological facilities through a "virtual laboratory". To this extent the partners have established databases of available resources and facilities, a model Material Transfer Agreement to regulate Intellectual Property issues, and a list of elements to consider for contracts between a visitor and a hosting facility. It was also important to agree on common sets of rules regarding experimental procedures such as Good Laboratory Practices (GLP), Standard Operating Procedures (SOP) and Quality Assurance/ Quality Control (QA/QC).

Oligo arrays

In order to produce comparable results within the Network it was highly desirable for EADGENE partners to conduct their experiments using microarrays from the same sources. Therefore, EADGENE has invested in chicken, pig and bovine oligo microarrays which are now produced within partner institutes and distributed to partners on request:

- *Chicken oligo array*: ARK Genomics, The Roslin Institute and R(D)SVS, University of Edinburgh (UEDIN), UK and CRB-Gadie, INRA Jouy-en-Josas, France
- *Bovine oligo array*: ARK Genomics, The Roslin Institute and R(D)SVS, University of Edinburgh, UK
- *Pig oligo array*: University of Aarhus (AV), Denmark and CRB-Gadie, INRA Jouy-en-Josas, France

Available collections

Next to the oligo arrays (see box), various other collections are available to the EADGENE partners: sources of microarrays for salmonids, E. coli and Salmonella, high-quality collections of microbes and bacterial pathogens, collections of clones from genomic and cDNA libraries of various sources and individuals, and samples from animal selection lines.

Reproducability of transcriptomic profiling

Three partners (INRA, UEDIN, AU) have conducted a microarray Quality Control (QC) study of the reproducibility of transcriptomic profiling experimental results between their laboratories. The fundamental idea of the QC experiment was to repeat the same experiment in three different laboratories using identical microarrays and aliquots of the same RNA samples.

The experiments were conducted using laboratory-specific protocols for labelling, hybridisation, washing and scanning, which all differed between the laboratories. This "technological triangle" aims to share experiences, ideas, methods etc. and thereby further stimulate the interactions between the institutions. The EADGENE interactions on transcriptomics technology will continue and are moving into high throughput sequencing.

Bioinformatics Tools for Biologists

Christophe Klopp, INRA, France

Genome sequences, cDNA resources, and micro-array expression studies all involve the generation of thousands if not millions of data points. It is essential that these data are handled correctly and made available to the wider scientific community in a user-friendly format, conducive to furthering the understanding of the biological systems being investigated. Therefore, up-to-date bioinformatics tools are critical in all studies including genomic data types.

One of the major contributions from EADGENE's bioinformatics group has been the production of up-to-date annotation files, allowing the extraction of biological knowledge from the microarray experiment results (see 'Virtual Lab').

Annotation files

Annotation files (chicken, pig and bovine) can now be downloaded from the EADGENE website. File data and formats have been adapted to the users' needs according to feedback received. Also, a kind of "identity card" of the oligo-sets goes with these annotation files, which is intended to help the biologists choose between oligo-sets when they start a new experiment. This two page description gives information about the size of the set, the number of oligos which have been annotated, and how precisely they match the corresponding genes. It also indicates how many of the genes have human or mouse orthologues, the IDs of which are commonly used to retrieve data from biological network software like Ingenuity Pathway Analysis Software or Genomatics.

Annotation events

EADGENE has organised, in cooperation with SABRE, two annotation events.

1. Microarray Annotation Workshop

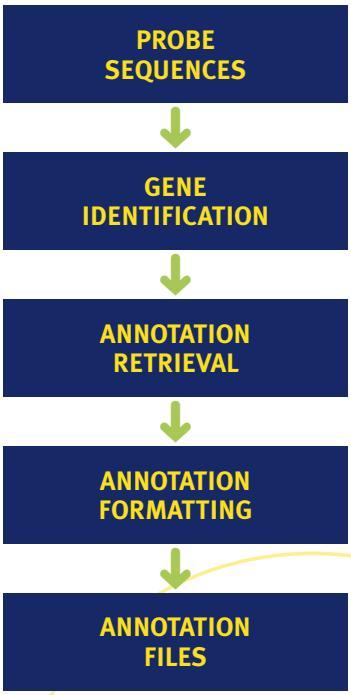
The aims of the workshop were: (i) to present the different annotation strategies and tools; and (ii) to compare the resulting annotations of a common set of oligos which were distributed to participants prior to the meeting. The results gave the biologists a good insight into these oligo-sets, by analysing the specificity of each probe versus the corresponding transcriptome and genome. Another result was the highlighting of possible oligo design caveats like retained introns or transcriptome fragment banks artefacts.

2. Cattle annotation jamboree

When the bovine genome sequence came available, genes, transcripts and other features were annotated onto the sequence. The positions of genes is valuable information for biological research and indispensable for applications such as comparative genomics, fine-mapping of quantitative trait loci and interpretation of microarray experiments. The available software to annotate ('cottage model') was complicated – therefore Europe organised an annotation jamboree in Hinxton, with the Sanger Institute HAVANA group aiding, and funding provided from EADGENE and SABRE. 474 transcripts were manually added on a total of 153 scaffolds by biology-oriented experts.

Annotation

Annotation is the process of giving a recognisable gene id (or label) which will identifying the gene which is targeted by a given probe on the microarray. Genomic information is continually evolving as new genome assembly versions are published, new gene build versions are issued, etc. In addition, annotation information is continually being updated as new information on gene ontologies, orthologous genes, biological pathways, etc. becomes available to the scientific community.



Re-annotation pipeline

Sharing Analytical Tools

Dirk-Jan de Koning, The Roslin Institute and R(D)SVS, University of Edinburgh, UK

The EADGENE Analytical Tools Group shares expertise from throughout the Network to provide practical solutions and guidance for analysis of animal disease genomics data. The work of this group is very much demand-led, based on an initial survey, with new topics added as the technologies and the analysis methods have evolved: a training course for the design and statistical analysis of micro-array experiments, that is being given regularly, a workshop on the analysis of micro-array data, a joint EADGENE-SABRE working group on post-analyses of micro-array data, and a workshop on bioinformatics and data handling methods. The successes of this group can be attributed to the willing cooperation and active participation of the various researchers from our EADGENE partner institutes, and the willingness of research groups to share their data and results. In particular, the publication of 19 scientific papers provides a concrete and long-lasting output from this group and is a good example of the collaborative work that can take place within a Network of Excellence.

Micro-array Training Course

EADGENE has developed a training course for research scientists, on the design and statistical analysis of micro-array experiments. The course has been given three times, and will continue in the future. Micro-arrays have a number of set stages: experimental design, image analysis, removal of outlier slides, normalisation, statistical analysis of gene expression, and interpretation and reporting of results. The 3-day course is designed to address each of these issues, and provide the students with approaches and strategies to cope with each stage.

Three other Workshops Cross-foster Expertise

Animal disease data presents many challenges, so specialists with expertise in both animal health and data analysis are needed to design experiments and interpret the data, and to translate the results to industry. In 2007, the workshop "From Infection to Inference: Interpreting Animal Health and Disease Data" enhanced the dialogue between disease and data.

Bioinformatics & Data Handling

In 2009, a workshop around bioinformatics and data handling focused on the scientists' experiences of a variety of bioinformatics and data handling methods for next-generation sequencing data. These new generation sequencing technologies, where a single machine can rapidly sequence several genomes, have greatly increased the amount of data to be handled by bioinformatics, and this presents scientists with fresh challenges.

Field Disease Data

In 2010, a workshop has been held on the design, collection and analysis of field disease data, with the objective of developing a blueprint for the design and analysis of disease genetic studies using field data.

Microarray Workshops

The first workshop focussed on the statistical analysis of microarray experiments from raw data to gene list. Prior to the workshop, the participants received a set of real and simulated microarray data, which they analysed according to their preferred methodology. The real data came from an EADGENE mastitis working group study looking at gene expression changes following artificial infection with two different strains of mastitis causing bacteria, and included several time-points, resulting in a true analytical challenge (48 microarrays). Participants were expected to deliver a list of differentially expressed genes. The simulated data showed that despite very different approaches nearly all groups correctly identified their best 250 genes as differentially expressed. The results were fed back to the mastitis WG, and published in 4 EADGENE papers in Genet. Sel. Evol. 39 (2007) 621-683.

The second workshop focused on the post-analyses of gene expression experiments in collaboration with SABRE. Using both SABRE and EADGENE results, the following topics were addressed: 1) re-annotation of the probe set on DNA microarrays, 2) pathway analyses to identify significantly affected biological processes from microarray results, 3) reverse engineering of regulatory networks from microarray results, 4) the integration of gene expression studies with QTL detection studies and 5) the prediction of phenotypic outcomes using gene expression results.

This resulted in 15 EADGENE papers in BMC Proceedings 3 (2009) Suppl. 4.

Structural Genomics

Martien Groenen, Wageningen University, Wageningen UR, The Netherlands

The Structural Genomics work in EADGENE positioned Europe in genome sequencing and annotation. It has ensured a strong position for the research groups involved in EADGENE within international worldwide collaborations to establish and improve the genome sequences and their annotations of many livestock species. From the start, a characteristic of this work therefore has been its strong connection with other international projects often co-funded by a large number of national funding agencies, and, importantly, with the bioinformatics work in EADGENE. The majority of the work concerned the major livestock species such as chicken, pig and cow, but progress was achieved for salmon and turkey as well. For instance miRNAs in chicken and ruminants, and, SNPs and CNV in chicken and turkey. Although the emphasis has been on the host species, considerable progress has been made also in the further characterisation of the genomes of a number of pathogens including Salmonella enterica, Eimeria tenella and Mycoplasma agalctiae.

Improved Genome Annotations

CHICKEN

Improved annotation of genes involved in immunity. Genes involved in immunity are in general characterised by their relative fast evolutionary rates, making it more difficult to identify orthologous relationships between these genes within species that have diverged over considerable times like birds and mammals.

CATTLE

In the context of the international consortium for sequencing the bovine genome, the consistency of the two different assemblies produced was checked, using RH maps based on genotype data from the Illumina bovine SNP50 Beadchip.

SALMON

Because no genome sequencing initiative had been started for salmon, this work mainly concentrated on the development of EST resources in salmon and the development of SNP markers and microarrays based on these EST resources.

PATHOGENS

The genomes of Salmonella enterica and other Salmonella species were analysed in more detail via a comparative genomics approach to identify fimbrial operons, phages and pathogenecity islands. Furthermore, the annotation of the Eimeria genome was improved by establishing 3,000 manual gene annotations and over 40,000 in silico gene predictions, including EST gene builds.

Programmes and web browsers to aid in the visualisation, annotation and analysis of genome sequences

http://bioinfo.genopole-toulouse.prd.fr/narcisse/
to display the comparisons between complete genome sequences.

Coxpress (IAH)
freely available programme for the further improvement of the annotation of genes in species whose genome is already available (i.e. chicken and cow).

Other
web front-end access programmes MLAGAN and MAVID for biologist end-users, and software, TBA and PECAN
(*http://www.ebi.ac.uk/~bjp/pecan*).

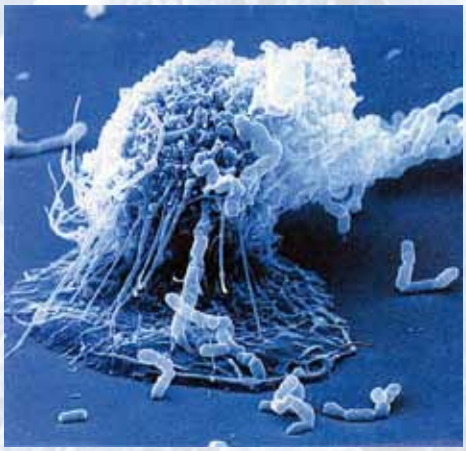
Salmonella Working Group

Annemarie Rebel, Animal Sciences Group, Wageningen UR, The Netherlands

EADGENE Pathogen WGs

EADGENE has created Pathogen Working Groups to combine the numerous efforts in pathogen research across various host species. These successful WGs have combined the cross cutting expertise of host and pathogen, enabling the comparison and optimisation of various methods, and findings.

Different animal lines have different responses to a Salmonella infection. The reasons can be different susceptibility of the gut, differences in the clearance of the Salmonella from the animal, or in different systemic response, also the animal reacts different when other Salmonella species are the source of infection. We can obtain a better understanding of these processes if we investigate the differences and similarities in gene expression. The Salmonella WG has worked on the gut response, and the systemic response, and identified different responses between pigs and poultry, and to different Salmonella strains. The WG have met several times, also with the SABRE salmonella group, exchanged Salmonella strains, PCR primers, protocols to isolate Salmonella RNA and protocols to culture pig intestinal cells, which took place in order to overcome major differences between institutes. The use of different lines and species of animals and the use of different Salmonella species was encouraged so that more information about host response to Salmonella infection could be obtained.



Host response upon a Salmonella infection: was investigated with in vitro and in vivo models, and using different strains of Salmonella. The lists of the "top 5" induced genes after Salmonella infection of the partners were combined to depict genes that were found to be regulated in the different infection models within different species (chickens, cattle and pigs). TLR4 was often found.

Salmonella response after interaction with a host: was investigated comparing the work on an in vitro model, with the material collected in in vivo experiments – problems with isolating bacterial RNA out of the already collected in vivo samples made this impossible.

Identification of specific cells which react after infection: was investigated in various ways, e.g. by obtaining cells, such as neutrophils, from animals and measuring the response after an in vitro infection, via q-PCR, microarrays or protein analyses. The results were related back to the host response upon a Salmonella infection.

Combining results of different infection models, species, and salmonella strains: led to the composition of an additional proposal. Also, different salmonella strains were used in an in vitro model of HD-11 cells of chicken origin and the results from the various partners working on this will be combined in the near future.

Fish Pathogen Working Group

Bjørn Høyheim, Norwegian School of Veterinary Science, Norway

The EADGENE Fish Pathogen Working Group combines expertise genomics and immunology in fish host and pathogen.

The host focus was on salmonids **(Atlantic salmon and rainbow trout)**. Salmonids are of high commercial value in Europe. Both salmon and trout are have been used extensively for genome studies – both species have a large degree of genetic similarity between the them, i.e. genetic markers and micro-array chips developed for one species can often be used on the other.

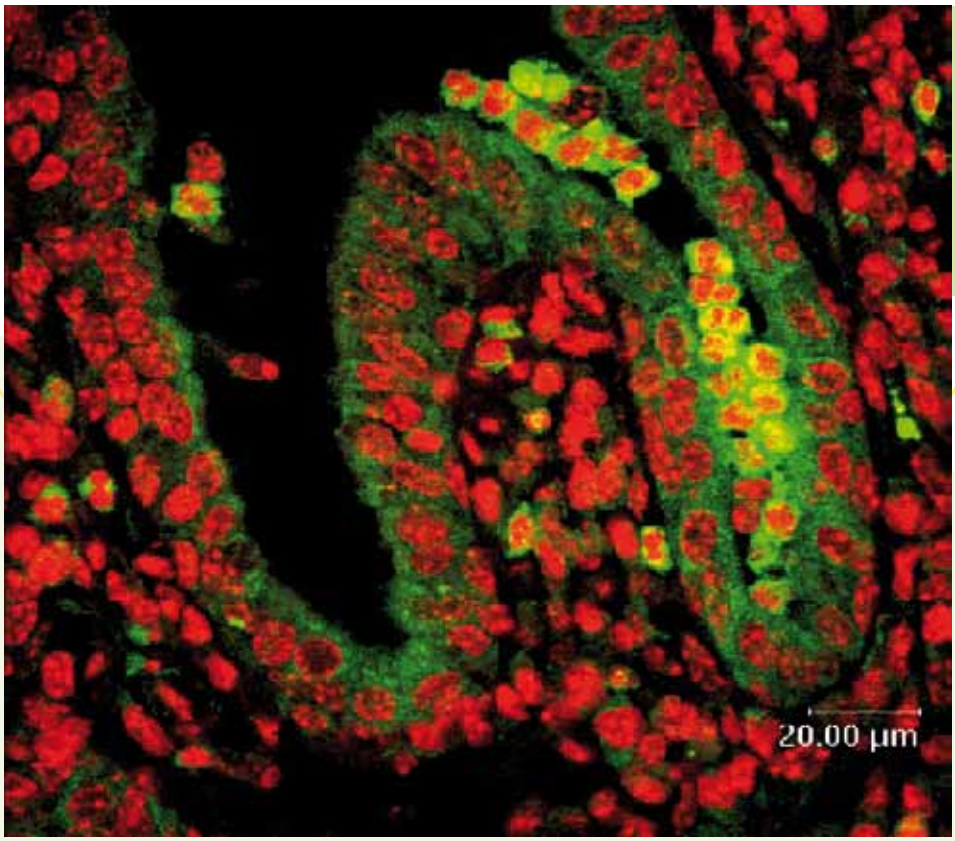
The impact of viral diseases represents a major economic cost- the working group focused on: **Infectious Salmon Anaemia virus** (ISAV) and **Infectious Pancreatic Necrosis Virus** (IPNV). There are good challenge models for both viruses. To investigate the host response to ISAV and IPNV, genome scans of Atlantic salmon challenged with IPNV, and transcriptome analysis on both Atlantic salmon (AS) and rainbow trout (RT) challenged with ISAV (AS and RT) and IPNV (AS), were performed. The genome scans identified the position of the QTLs both in seawater (post-smolt) and the freshwater/fry (pre-smolt) stage of the lifecycle. The most significant QTL was found in the same region on LG 21 in both instances, and explains the majority of the genetic variation in resistance to IPN. Several **transcriptome studies** have been carried out to identify candidate genes. Both differential expression and microarray experiments have been completed on salmon challenged with ISAV, resulting in identification of a set of genes that are differentially transcribed after infection. This includes among others immune-related and other genes. Further work should uncover the roles of the differentially regulated transcripts/genes in infection and immunity. Transcriptome studies involving Atlantic salmon challenged with IPNV and rainbow trout challenged with ISAV are underway.

The **genome of ISAV has been entirely sequenced**, and reverse genetics of ISAV after infection of rainbow trout has been completed . This opens up the possibility of a more detailed study of the host/pathogen interaction during infection.

The work on **viral haemorrhagic septicaemia virus** (VHSV) has shown that gene expression profiles differ between the resistant and the susceptible trout families.(both in timing and quantitiy of up- and down regulation of genes). Isolation and characterisation of three key factors of **innate immunity from rainbow trout** (MyD88, Tollip, and amyloid A) reveals that these factors share a remarkable high degree of structural conservation with their mammalian orthologs suggesting that innate immune defence mechanisms are conserved over a period of more than 450M years, when piscine and mammalian lineage separated.

Mastitis Working Group

Hans-Martin Seyfert, Leibniz Institute for Farm Animal Biology (FBN), Germany



Section through an udder quarter sampled 24h after infection with E. coli. Green fluorescence indicates expression of the bactericidal ß-defensin peptide LAP. Nuclei are stained in red.

The **EADGENE Mastitis Working Group** has brought together the research activities and results from institutes located in seven European countries, working on **mastitis in cattle, goats and sheep**. Immune defence in the udder is organ specific, but is also modulated by the species of the host. The mastitis working group characterises the genetic basis of host specific properties of udder defence, using both in vivo and in vitro techniques. With whole genome covering transcriptome profilings key genes were identified in udder and immune cells counteracting the attack of three pathogens: **Escherichia coli, Staphylococcus aureus or Streptococcus uberis**. The contribution of milk cells to counteract S. aureus infections of goat udders was also recorded. Selection lines with differing genetic predisposition for suffering from mastitis were established in sheep and the selection line specific response of their milk cells towards an S. aureus challenge has been recorded.

The data were exploited in different ways: a large dataset was used to to evaluate the power and robustness of different biostatistical tools (see Microarray Data Analysis Workshop), resulting in guidelines for proper data handling. Based on these experiences the data are currently being exploited for gene mining in different ways. Biostatistical and bioinformatical tools are being used to identify host genes contributing to the pathogen-specific, and eventually udder or cell type specific immune response. The data have also been used for hypothesis driven analysis into organ specific immune mechanisms and their pathogen-specific modulation. The mastitis data have furthermore been utilised as input by the Operational Genomics Working Group.

Operational Genomics Working Group

Elisabetta Giuffra, Parco Tecnologico Padano, Italy

A meta-analysis of the various mastitis experiments via the Pointillist (Hwang et al. 2005 Proc. Natl. Acad. Sci. 102, 17302-7 and 17296-301) meta-analysis tool was performed to deal effectively with the high heterogeneity of the final dataset, analysing the 11 gene lists obtained (bovine, goat, resp sheep specific; general overall, early and late time response; early and late time specific; general, early and late time in vitro response) to infer which genes and gene pathways were modulated in different mastitis biological systems. In this way important features could be identified (Genini et al. in preparation), for instance: a) Despite the small number of genes (7221) common between the different types of arrays used, the **immune response** was the most significant commonality emerging from the global dataset, and of the bovine specific response (based on 19452 genes). b) the pattern of up- or down-regulation is generally uniform across experiments. (e.g. bovine in vivo experiments: see figure 1). The meta-analysis highlighted **pathogen specific response signatures** for E. coli, S. aureus and S. uberis, e.g. the magnitude of inflammation induced by the E. coli challenge is stronger than the one induced by S. aureus.

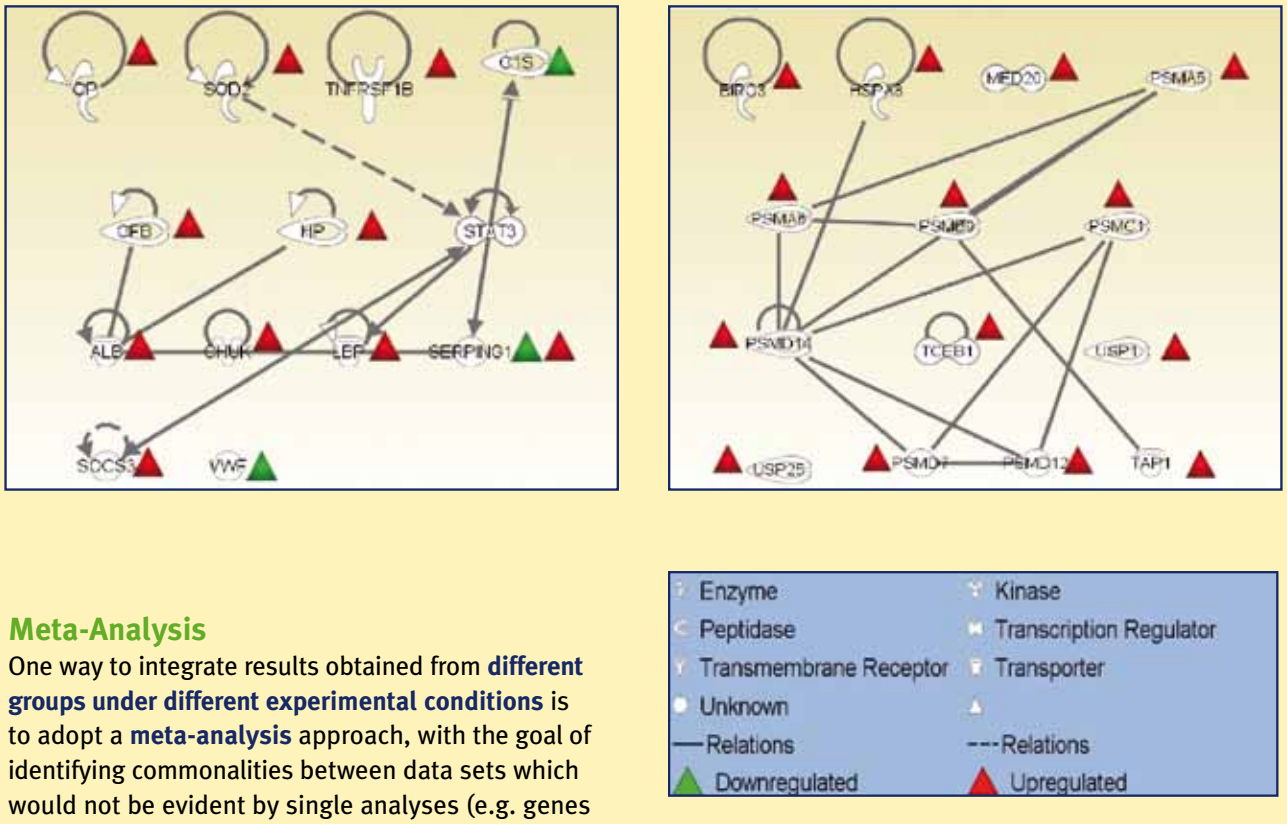


Figure 1: Direction of change of the genes belonging to two canonical pathways inferred by meta-analysis of the bovine microarray datasets.
***A:** Acute phase response, **B:** protein ubiquitation*

Meta-Analysis

One way to integrate results obtained from **different groups under different experimental conditions** is to adopt a **meta-analysis** approach, with the goal of identifying commonalities between data sets which would not be evident by single analyses (e.g. genes commonly induced by a pathological state). This is possible thanks to the higher statistical power and diminution of false positives which are obtained when data sets are integrated by meta-analysis.

Industry Working Groups and Projects

Marjolein Neuteboom, European Forum of Farm Animal Breeders

Industry – research relations have been an important part of the EADGENE Network of Excellence.

Club of Interest

A club of interested industries has been formed around EADGENE and has provided the basis for the technology implementation related activities. Their particularities have been mapped by extensive enquiries, as well as their needs, possible animal populations and other material of interest.

Industry Days

Two successful "Industry Days" conferences were organised (one together with SABRE). They consisted of industry/research presentations, highlighting results and outlooks of interest for industry.

Technology Transfer Visits and Industry Participation in EADGENE Working Group Meetings

The EFFAB Technology Transfer Facilitators (TTFs) have visited companies across Europe setting up links between the EADGENE research partners and industry, mapping the needs within animal health genomics, and identifying gaps in order to enhance animal health implementation. Numerous industry-research co-operations have been initiated through these visits; the visits were especially important for linking partners across countries, across species, or between fields of business/research that had not been linked before. TTFs are independent experts, able to make links between groups independently, not marketing one research organisation, nor one country, nor one industry. Industry was invited and participated to various working group meetings of EADGENE – this has resulted in fruitful new projects and industry-research collaborations on animal health genomics.

Knowledge Management and Technology Transfer Industry Expert Groups:

During the first 18 months of the project two working groups of industry experts developed technology transfer guidelines and advised on contracts for industry–research cooperation in animal genomics. They also developed the concept of the industry days.

The Technology Transfer Guidelines focus on and highlight the benefits for each of the partners of collaboration between industry and research, as the major incentive to bridge the technology transfer gap.

An extensive Do's and Don'ts protocol for Technology Transfer has been set up as a guide for research institutes, scientists, and industry with the objective of making them aware of common problems, so that efficient collaborative research activities can be established efficiently in the framework of current legislation. It contains several documents which can be of great help when setting up cooperations between industry and research institutes.

Animal Health Data Comparison across Countries

Genomics needs phenotypic data, but animal health data is scattered through Europe over a broad range of companies and institutes. Sensitivities and issues over ownership of the data make it especially difficult to bring these data together on a large scale. The AHDC project has mapped the existing data systems within pilot countries (UK, FR, NL, DK) and their particularities. Stakeholders have been meeting in two workshops to define the way forward. Different pathways per species prove necessary – working groups on pig, poultry and cattle are now defining the follow up phase. There is a lot of interest from different parties, including DG Sanco, Copa-Cogeca, OIE, European Pig Producers, ICAR, to work towards a more comparable animal health data system in Europe (www.eadgene.info ⇢ Industry ⇢ Data Comparison).

Phenotypic Database

The phenotypic database has been developed to provide a virtual place were industry can indicate what material they wish to bring into pre-competitive scientific research. It is one of the outputs based on the inquiry amongst the Club of Interest in year 1. This database provides researchers with a unique opportunity to search for possible partners from industry, and provides lots of benefits for both parties in terms of connections and collaborations. An updated version which will make it even more easy to find the right information is being integrated in the EADGENE website.

Ontology Project

A worldwide ontology for genetics and genomics is currently being set-up. To be able to pick up developments without delay it is important for industry to link their traits and definitions to their work timely and in a coherent way. For everybody, the process of collecting these is time consuming, with repetitions and risk of errors. A free tool has been developed which allows the adding of traits and other information in a very structured manner. It takes away the need to add similar traits for every species or purpose. The tool is almost finished, collected traits will be entered. A follow up project proposal is underway, links with the INRA ontology project are being made.

Poultry Disease Projects for Industry

Olivier Demeure and Fanny Calenge, INRA, France

Laying hen

Technology transfer poultry projects

Technology transfer between science and industry is a particular priority for EADGENE. The technology transfer poultry projects are guided by a working group with equal numbers of representatives from science and industry.
The research proposals were optimised with input from industry, the industry participants have been updated regularly with progress and results, and they could give their input to the project.
The researchers have used commercial lines, bringing the research closer to industry practice. Both industry and research see this project as a win-win situation - it provides useful research for industry and the commercial lines needed to continue their work for the scientists. Research and an animal breeder continue in a follow-up excercise.

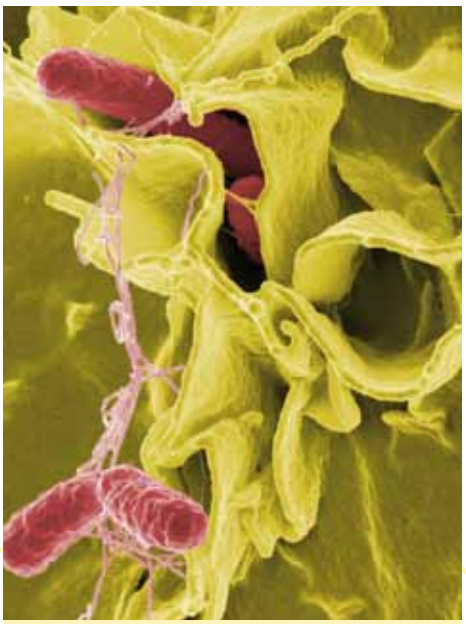
Project 1: Epistasis effects on resistance to disease traits in chicken

2380 animals with phenotypes for disease, composition or quality traits have been genotyped by 1536 SNPs selected using MarkerSet (Demeure and Lecerf, 2008). The first QTL analyses were using QTLMAP which has been adapted to handle large number of markers. Finally, 56 QTLs affecting traits related to coccidiosis resistance and more than 90 QTLs affecting growth, body composition or quality related traits were identified. The testing of different methods for epistasis analysis to estimate the impact on these traits is under progress. Results will then be transferred to a high quality, slow growing commercial line targeting the previously detected regions by genotyping 1000 animals (10 families) for 384 SNP.

Project 2: SNP markers associated with resistance to Salmonella

1536 SNP were chosen. 194 of them had been formerly identified within the three QTL regions (GGA1, GGA2, GGA5) known for their effect on resistance to Salmonella carrier-state. Indeed GGA1 has been confirmed in these commercial lines at the younger age, GGA2 has been confirmed in the F2 cross between the inbred N and 6 lines (Calenge et al., 2009) and it has been shown that GGA5 is close to Sal1. The other 1342 SNPs were chosen for their informativity giving a good coverage of the rest of the genome. This SNP set has been used to genotype 650 animals measured for resistance to Salmonella carrier-state, either at a younger age (at 1 week of age, to mimic infection of broilers) or at the adult age (at the peak of lay when hens may lay contaminated eggs which are the main source of human toxi-infections). Consideration of both traits is of importance since they appear to be negatively and moderately genetically correlated (Beaumont et al., 2009). A statistical evaluation of each SNP effect on carrier state and of each animal's genetic value has completed the project.

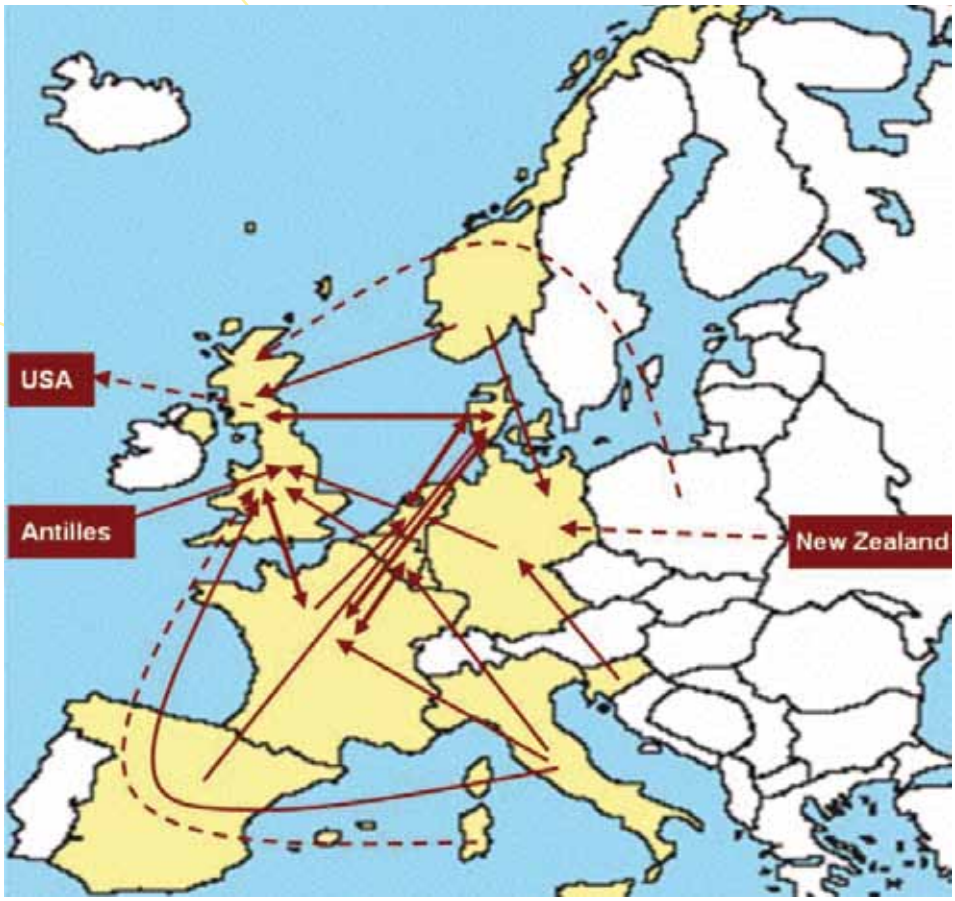
For **further information** please visit **www.eadgene.info** ⇢ Industry



Pathogens interact with host cell

Facilitating the Exchange of Ideas and Expertise

Hans-Martin Seyfert, Leibniz Institute for Farm Animal Biology (FBN), Germany



A key method of increasing cooperation between institutes is to facilitate **short-term stays** (up to 3 months) of scientists at other organisations, allowing the face-to-face exchange of ideas and technical expertise, and fostering long-term research collaborations. EADGENE has developed an easy-to-follow scheme to file applications - a **"Mobility Centre"** on the EADGENE web-site. All applications are independently evaluated by three reviewers and the financial support is awarded to successful applicants as a stipend.

The EADGENE short-term stay (STS) funding instrument has been highly successful in enabling motivated researchers to visit other organisations within the 15 EADGENE partner institutes, and also other institutes, including some in the USA, Japan and Australia. Twelve of the 15 EADGENE members and 13 non-members, including Eastern European Countries, have sent or received visiting scientists. These visits include exchanges of senior scientific staff, as well as post-docs and students.

The STS programme has been a continual success throughout the project. To date there have been **49 STS visits** funded with a total of **120,184€** (see figure2). Recipients of EADGENE short-term stay funding write short reports upon completion of their visits and these are added to the EADGENE web-site (**www.eadgene.info** ⇢ Training & Careers ⇢ Short-term Stay Results & Reports). The results of STS visits have also been featured at EADGENE's annual conferences in 2006, 2007, 2008 and 2009.

Figure 2: Number of STS awards.

Increasing Skills through Training

Diego Llanes, University of Cordoba, Spain

Laboratories involved in the EADGENE Network have extensive experience in organising scientific training at a number of levels, ranging from the individual training of students and visiting workers, through organised workshops, to specific training modules focussed on particular scientific topics. Over the last five years EADGENE has been involved in **developing and funding new courses and promoting and sponsoring existing courses**. Educational materials such as bibliographies and protocols from courses are available from the **training pages of the EADGENE website** (**http://www.eadgene.info** ⇢ Training and Careers).

In addition to short courses and workshops, EADGENE has promoted longer-term courses, such as the 2-year European Master in Animal Breeding and Genetics (EM-ABG), under the Erasmus Mundus Programme. This course is co-ordinated by an EADGENE Partner, Wageningen University, and involves five other universities from across Europe. EADGENE has been successful in creating a **Collaborative Group on Animal Genomics Training within Veterinary Faculties** from members of the EADGENE Network: University of Cordoba, Norwegian School of Veterinary Science, University of Liège, Ecole Vétérinaire of Toulouse and University of Ljubljana. This group will offer a framework for training in animal genomics and health as part of the veterinary studies under the Erasmus programme. The aim is to establish a shared resource for training in the field of genomics for host-pathogen interactions, which could later possibly be expanded by making course materials available to animal science and agriculture courses at other institutions.

Practical session at the EADGENE Microarray Data Analysis and Meta-Analysis Course

EADGENE Training Courses

- European Institute for Statistical Genetics (Sept 2009, Sept 2007)
- QTL-MAS Workshops (Apr 2009, May 2008)
- Study of Resistance Mechanisms in Animal Infectious Diseases (Mar 2009, Nov 2006)
- Cytoscape Software (Nov 2008)
- Microarray Data Analysis & Meta-Analysis (Oct 2008, May 2006, Dec 2005)
- miRNAs Workshop (May 2008)
- New Insights into Mixed Model Methodology with Applications to Genomics & Biostatistics (May 2007)
- Microarray Course (Nov 2006)
- cDNA Microarrays: Experimental Procedures and Data Analysis (Oct 2005)
- Genomics for Beginners (Oct 2005)

Ethical Deliberation within EADGENE

C. Gamborg, K. Klint Jensen, G. Meyer, P. Sandøe, Danish Centre for Bioethics and Risk Assessment, University of Copenhagen, Denmark

Interviews and workshops

After an analysis of basic EADGENE documents, a series of interviews with individual EADGENE researchers was used as the point of departure for suggesting a set of principles for ethical deliberation within the network and in public: moderation, openness, animal welfare as a research purpose and a goal in its own right, and continuous reflection on responsibilities. The third approach consisted of a series of workshops, involving network participants in discussions structured by the ethical matrix – a conceptual tool for supporting discussions on ethics and technology. Used as a framework for reflection, the ethical matrix is aimed at furthering exchanges between different points of view and at forcing participants to explicit ethical reasoning. Six workshops were arranged, including four regional workshops, using local cases as their starting point, and one external stakeholder workshop (organised in cooperation with Kate Millar, University of Nottingham).

	Respect for		
Interest group	**WELL-BEING**	**AUTONOMY**	**JUSTICE**
PRODUCERS/INDUSTRY			
CONSUMERS/CITIZENS			
SCIENTISTS			
ANIMALS IN RESEARCH			
PRODUCTION ANIMALS			
ENVIRONMENT			

Ethical Matrix modified for EADGENE

EADGENE has identified **ethical challenges, relevant to research in the field of animal disease genomics**. Regardless of the approach – and very different methods have been used – key ethical challenges have consistently been identified as relating to vested interests, to communication with the public at large, and to the question of how to combine the use of animals with care and concern for animals in their own right.
Demands from the workshops have resulted in the production of a set of internal research guidelines for experiments on animals, and an on-line manual for ethical reflection, e.g. a report on perceptions among external stakeholders, and an implementation strategy regarding ethical and societal issues.
A paper reporting the workshops and the outcome of the ethical deliberations has been accepted for publication in an international peer-reviewed journal (Science and Engineering Ethics).

Three major issues

The first major area of interest – **how to cope with vested interests and conflicts of interest** – has been discussed in relation to the growing prominence of intellectual property rights in the field of biotechnology. This is an area of outspoken disagreement both in society at large and among scientists in general, EADGENE participants included. In practice, a dilemma is often experienced between a general principle of openness and demands for confidentiality when a process of patenting is ongoing. Discussions have been hampered by a lack of established routines for coping with social interests within, and not just outside, the world of scientific research.

Ethical Deliberation within EADGENE

Exchanges within the network on the second issue, concerning **relations with the public at large**, have consistently been characterised by ambiguity. Basically, arguments have been put from two different positions. In one position, arguments are based on the assumption that the main purpose of communication is to gain trust, educate and convince the public at large about the rightful aims of the research project. The internal sphere of science is taken to be clearly separated from the external, public sphere. Another position, which has been much less explicit and clear-cut in interviews and at workshops, tends to combine internal reflection and discussions on the mores and means of the research with a broader societal discussion.

The challenge of **combining the use of animals with concern and care for animals** in their own right is the third major ethical issue that has remained on lists of ethical challenges throughout the project. In the initial reports, concerns regarding production animals were in focus, and it was suggested that the relationship between the economic interests of breeders and farmers, on the one hand, and the welfare of production animals, on the other, should be presented as issues for reflection within the network. At the internal workshops, attention was given to the conditions of the research animals. However, there was also concern about the risk that breeding for more robust animals might not materialise in better conditions for future productions animals. At the external stakeholders' workshop, this concern reappeared as an ethical issue.

Lessons learned

Ethical challenges may be acted upon in a variety of ways and at different levels. At one level, internal reflection and exchanges may be stimulated. At another level, internal policies, rules and routines may be altered. And at yet another level, problems that seem to go beyond the scope of an individual project may be taken to the public sphere/and or to public authorities. The practical impact in the case of EADGENE has so far remained largely at the first level.

Discussions at the workshops and feedback forms completed by participants indicate that **the goal of raising awareness with respect to ethical challenges has been reached**. Thus, the ethical matrix may serve to structure discussions, but care should be taken to use it only as a starting point and an initial frame for discussions, not as an end in itself. The direct link to the actual research projects of the participants – as distinct from general ethics teaching – is important to make ethical reflection seem relevant to the researchers. At the same time, however, the challenge of meeting society at large in an informed and value based dialogue remains. It remains a challenge to consider how reflection and deliberation on ethical issues may and should affect the actual policies and management of research projects.

Communicating EADGENE's Results

Caroline Channing, The Roslin Institute and R(D)SVS, University of Edinburgh,UK

EADGENE has communicated its results in various ways to the general public, scientific groups and industrial communities.

Newsletters

EADGENE publishes two newsletters, "EADGENE News" for the general public and industry, and "Network News" for the EADGENE Partners. They have been issued three times a year, and can be downloaded from **www.eadgene.info** ⇢ News & Publications.

Scientific Publications

Peer-reviewed scientific papers provide a concrete and lasting output from any scientific project. EADGENE has not only funded the research reported in these papers, but has also helped bring scientists together in working groups which have produced multi-partner papers, and has paid for publications to be made open-access for everyone through online journals. A list of EADGENE publications can be found on **www.eadgene.info** ⇢ News & Publications.

Conferences, workshops and meetings

EADGENE has held annual conferences in partner countries every year since the start of the project. The annual EADGENE Days conferences have been very popular and have helped increase the knowledge, understanding and recognition of EADGENE among relevant scientific and industrial communities through the presentation of EADGENE's research results. The communication of the results presented at these conferences continues through the conference pages

on the EADGENE website (**www.eadgene.info** ⇢ Events). EADGENE has also organised numerous workshops on topics such as analytical tools, specific diseases (mastitis, E. coli, Salmonella, fish pathogens), and ethics, and has organised satellite workshops and sessions at major international conferences (e.g. the EAAP conferences).

WWW.EADGENE.INFO

The EADGENE website provides information for the general public, industry and scientists on EADGENE's research, news, events, training courses, career opportunities and other information relevant to the EADGENE project.
The secure Intranet area for EADGENE's partners enables working groups and partners to exchange and communicate easily.

Promotional materials and communication tools

The EADGENE Communication Team has provided EADGENE's scientists with promotional materials (e.g. posters and leaflets), tools (e.g. online meeting tools, templates) and guidance, to encourage the open flow of communication and help them to promote the achievements of the EADGENE Network.

EADGENE Annual Conferences

- **Brussels 2005:**
  "EADGENE – its possibilities and its possible applications"
- **Oslo 2006:**
  "EADGENE Days 2006"
- **Utrecht 2007:**
  "Genomics for Animal Health"
- **Edinburgh 2008:**
  "Animal Disease Genomics: Opportunities and Applications"

EADGENE's Partners

EADGENE co-ordinates the host-pathogen genomics research activities of 15 organisations, from 10 European countries.

Institute National de la Recherche Agronomique (INRA), France
Wageningen Unversity (WUR), The Netherlands
Animal Science Group Lelystad (ASG-Lelystad), The Netherlands
Institute for Animal Health (IAH), UK
Roslin Institute and R(D)SVS, University of Edinburgh (UEDIN), UK
University of Aarhus Faculty of Agricultural Sciences (formerly DIAS), Denmark
Liege University, Belgium
Ljubljana University, Slovenia
Cordoba University, Spain
Norwegian School of Veterinary Science (NSVS), Norway
Leibniz Institute for Farm Animal Biology (FBN), Germany
Parco Tecnologico Padano (PTP), Italy
European Forum of Farm Animal Breeders (EFFAB)
University of Copenhagen (CeBRA), Denmark
Institute for Pig Genetics (IPG), The Netherlands

Co-ordinator: Marie-Hélène Pinard-van der Laan, UMR Génétique Animale et Biologie Intégrative - bât 211, Equipe Génétique, Immunité, Santé, INRA - Dépt. de Génétique Animale, F-78352 Jouy-en Josas Cedex, France; **Email:** eadgene@dga.jouy.inra.fr; **Website:** www.eadgene.info. EADGENE is a Network of Excellence supported by funding under the 6the Research Framework Programme of the European Commission. EU Contract No. Food-CT-2004-506416. This publication represents the vieuws of the Authors, not the EC. The EC is not liable for any use that may be made of the information.