



# INFLA-CARE e-Newsletter

The e-newsletter of the FP7-funded integrated project 'INFLA-CARE'



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## Note from the Project Coordinator

Welcome to the 2<sup>nd</sup> edition of the *INFLA-CARE* e-News letter, the publication of the European Commission funded research project *INFLA-CARE*. As *INFLA-CARE* continues in its final year, we feature more of our consortium members in this issue and list our current publications for the 2011-2012 period. Our editorial this time looks at the popular topic of **translational research** and we also have details of our forthcoming **Summer School** which will be held in Crete, Greece. I hope you enjoy our newsletter and that *INFLA-CARE* news will reach a wide audience who share an interest in our science.



Institute of Molecular Biology and Biotechnology (IMBB) Crete, Greece

Aris Eliopoulos, *INFLA-CARE* Co-ordinator,  
IMBB, Crete, Greece

## Meet our Team:

### 5 more members of INFLA-CARE come under the spotlight

**Moshe Oren** is based at the Weizmann Institute of Science in Israel, one of the world's foremost centres of scientific research and graduate study. Moshe is recognised as one of the world's leading scientists in the field of p53 research and his work gained the attention of the cancer research world in the early 1980s for his role in cloning p53, the 'tumour suppressor gene'.



Following a period as a visiting professor at Stanford University from 1988-1989, in 1993 he was appointed Director of the Leo and Julia Forchheimer Centre for Molecular Genetics at the Weizmann Institute, and he served as Dean of the Biology faculty at the Weizmann Institute from 1999-2003. In 2003 Moshe's research was recognised for its contribution to understanding the natural defence mechanisms against cancer and its potential to design better treatments; the highly selective MERIT (Method to Extend Research in Time) Award was granted by the National Institutes of Health (NIH) for 'long-term support to investigators with impressive records of scientific achievement in research areas of special importance or promise.'

The focus of Moshe's work at the Weizmann is the elucidation of the biochemical and biological processes that underlie the ability of p53 to act as a tumor suppressor, and more broadly, to explore the mechanistic links between regulation of gene expression and cancer. Moshe's lab also works on other proteins which interact with p53, such as the oncogene Mdm2 and tumour suppressors such as ARF and Lats2, microRNAs, mutant p53 gain of function and RNF20, an enzyme responsible for ubiquitination of histone H2B, which acts as a putative tumor suppressor through selective regulation of gene expression.

The **Almac Group** was established in 2001 and provides an extensive range of pharmaceutical services, from research, pharmaceutical and clinical development to product commercialisation. Almac's global headquarters are in Northern Ireland, UK and it has extensive facilities in the US. Almac has recently won a number of business awards for its excellence in the field of contract drug development and manufacturing within the biotechnology and pharmaceutical sectors. Over 600 companies worldwide use Almac's services which they tailor to meet client requests. The company

secured a prime position in the rapidly advancing field of genomic technology, being the first Affymetrix Service Provider in the world to gain ISO 17025 accreditation for Gene Expression and Bioinformatics services.

Almac Diagnostics has also established itself as a leader in scientific innovation: its unique range of Disease Specific Arrays (DSA™) research tools are the first microarrays available which are based on the transcriptome of an



individual disease. In the context of *INFLA-CARE*, Almac is assisting with the detailed experimental design, performance and data analysis of microarrays, aiming to define changes in the transcriptome during inflammation-driven cancer. The company is also involved in generating a liver cancer DSA designed to work with both fresh frozen and paraffin embedded tissue, enabling retrospective analysis.

**Manolis Pasparakis** did his Ph.D. thesis work in the lab of Dr. George Kollias, where he studied the role of TNF *in vivo* by generating and analysing TNF knockout mice. He received his Ph.D. in 1997 from the University of Athens and did his postdoctoral training in the lab of Professor Klaus Rajewsky at the Institute of Genetics, University of Cologne, Germany, where he studied the role of IKK subunits *in vivo* by generating and analyzing conditional knockout mice. After his postdoctoral studies he worked between 2002 and 2005 as a group leader at the EMBL Mouse



Biology Unit, Monterotondo, Italy, where his group generated a number of conditional knockout mouse strains and used them to dissect *in vivo* the role of IKK/NF- $\kappa$ B signalling in inflammatory conditions of the skin, liver and gastrointestinal tract. Since 2005 he has been a Professor at the Institute of Genetics, University of Cologne where his research focuses on studying the function of the IKK/NF- $\kappa$ B pathway and of TNFR and TLR signalling in the pathogenesis of inflammatory diseases and cancer.

**Josef Penninger** worked as a lead researcher at the Amgen Research Institute in Toronto affiliated with the University of Toronto and the Ontario Cancer Institute before accepting the appointment as director of the newly established Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA) in 2002. Currently, Josef is Adjunct Full Professor at the Department of Immunology, University of Toronto, Professor of Genetics at the University of Vienna, Austria, Honorary Professor of the Chinese Academy of Sciences/Peking Union Medical College and recipient of numerous awards and distinctions. Research in the Penninger lab at IMBA involves the genetic manipulation of genes in mice to determine the effects of mutations in the development of the whole organism and in diseases.



The interests of Josef's research group include heart and lung diseases, autoimmune diseases and cancers as well as bone diseases. The Penninger group has made a number of key findings in the fields of bone loss, bacterial infections linked to heart disease and cell signalling.

After a period of study at FDA - NIH, Bethesda, USA, **Mirco Ponzoni**



joined the Haematology and Oncology Department at the G. Gaslini Children's Hospital in 1987, where he directed a neuroblastoma research group whose work led

to two international clinical trials for Neuroblastoma patients. In the last 15 years, as director of the Experimental Therapy Laboratory of the G. Gaslini Children's Hospital, Mirco has developed new techniques for drug targeting, filing a series of patents for drug/gene delivery and tumour vascular targeting. Mirco and other members of his group have a very wide spectrum of technical expertise in nanotechnology, live cell imaging, cell and molecular biology, cancer biochemistry and novel experimental therapies for neuroectodermal tumors. As a partner of *INFLA-CARE*, Dr Ponzoni's group is involved in developing novel vehicles for the selective targeting of genes and cells responsible for triggering inflammation in various models of cancers.

## Editorial:Translational Research Mind the Gap

The pace of advances in molecular biology has been relentless over the last 40 years, driven by the pursuit of knowledge and the aim to understand and improve human health. Today's discoveries become a stepping stone for tomorrow's research; the number of scientific papers submitted for publication every year is huge and continues to grow, as do the number of journals willing to publish the results. Despite this golden age of biomedical research, the impact of all this knowledge on public health is modest; new effective cures and therapies are rare and our arsenal against major diseases is often outdated and only partly effective.

This discrepancy has been acknowledged by scientists and policy makers for at least a decade and **translational research** is seen by many to be the answer to this shortfall. In this article we look back at why translational research is deemed to be so important and whether it is really able to make a difference at the patient level.

Traditionally basic research has been performed in academic or specialist research institutions. The goal of scientists has been to publish their results with a meaningful commentary on their implications for the field. Drug companies however have remained separate entities, picking up potentially interesting results but only pursuing, manufacturing and marketing a selected few therapies on account of the cost involved and the potential for future revenue. The high price of many innovative drugs which eventually come on the market reflects the expense and risk of failure involved in the process of drug development.

Somewhere in between these two bastions of excellence is a no man's land which is the target of translational research and its development could deliver huge improvements in public health. Central to success in this approach is dynamic, early translational research which selects and transforms fundamental discoveries from the lab. These discoveries are then pursued in a focused way to ensure that the most promising aspects of research move forward with clearly defined milestones and goals. Importantly, this progress may be towards clinical goals rather than advances in scientific knowledge or developing new research opportunities. Following development in the lab, a potential therapy should have a smooth, timely transition to the various stages of clinical trials, commercialization and widespread use.

Unlike the traditional and practical aim of pharma companies to develop a new treatment which will get the best price when licenced, the aim of a translational research team is to make a discovery which will have a positive impact on public health at a more general level, regardless of potential revenues. By whittling down potential treatments at the earlier lab and clinical trial stages, new therapies can emerge for late stage clinical trials where they can then be pursued on a large scale by pharmaceuticals.

To achieve this however, translational research needs new experts to bridge the gap between academia and industry. Many academic scientists are reluctant to get involved in commercial activities which are often seen as a distraction from academic duties. Additionally, new infrastructure which was previously the domain of wealthy pharmaceutical companies is essential for the success of translational research. The wealth of basic scientific knowledge which is ripe for translation lies fallow without access to the critical infrastructure and state-of-the-art facilities which are essential to meet good manufacturing practice (GMP) standards required when making compounds for use in human clinical trials. Additionally, core services for translational research must be high quality, cost

effective and accessible for this approach to be effective.

The European Commission has illustrated its commitment to translational research by its investment in the FP7 initiative, a 50 billion euro programme over 7 years. Its objectives are to improve the health of European citizens and to increase the innovative capacity of European health industries and businesses. Clear designation of funding and co-ordination by the EC limits translational research duplication across Europe and results in a cohesive research effort which is constantly monitored by a regular review process. By placing the emphasis on funding translational research, the EC is investing in the development of new therapies and their validation - a long term strategy with the benefit of every European citizen in mind. Central to this strategy is the small to medium enterprise (SME) which the EC sees as the main economic drivers of health care, biotechnology and medical technologies. SME's can provide a vital link in pursuing new therapies by providing industry know-how and making industrial level technology available to research groups.

Whilst it is early to appraise the success of the translational research funded by the FP7 initiative, there are success stories for translational research from further afield. The rapid development of the innovative cancer

## Annual Meetings

*INFLA-CARE* last met in September 2011 in Athens, Greece for its **3<sup>rd</sup> annual meeting** which was well attended and enjoyed by the consortium. The SAB report on the progress of *INFLA-CARE* commented favourably on the breadth and depth of the work presented at the meeting. We received additional praise for the high quality of training of young researchers in the interface between inflammatory biology and cancer pathogenesis. In their summary, the SAB reflected on the success of the “outstanding

drug bortezomib by biotechnology company Myogenics/ProScrip began with academics from Harvard University and was made possible by a complex web of academia–industry/public sector–private sector interactions. Despite potentially significant obstacles such as intellectual property rights and the issue of which research direction to take- towards cancer, inflammation or muscle wasting-which threatened to delay or halt the progression of this research, bortezomib was launched as an effective treatment against multiple myeloma in record time. More details of this fascinating example of successful translation research can be read at [Sanchez-Serrano-NRDD-article.pdf](#)

The bortezomib story has also demonstrated that translational research isn't solely about the flow of potential benefits from the bench to the bedside. Important lessons have been learned when knowledge feeds back to the bench from observations at the clinical trial level, which can only help to expand our scientific knowledge and refine future therapies for the patient.

The future looks bright for both scientists and patients if the principles of translational research can be put into action. The vast array of intellectual riches from biomedical discoveries await the transformation into practical riches, from which patients and society as a whole can benefit.

group of (*INFLA-CARE*) investigators conducting world-class research” and wished the consortium well in the final year of the programme.

The **4<sup>th</sup> annual *INFLA-CARE* meeting** will be held on 23-24 September 2012, at the Ikaros Village Beach Resort and Spa, in Malia, Crete, Greece. This final meeting of *INFLA-CARE* members will provide an important and timely opportunity to review the progress of the consortium towards the end of the 4 year funding period. We hope that delegates at the meeting will enjoy their stay at one of the leading hotels on the island and we look forward

to hearing about the fruition of many aspects of *INFLA-CARE* research.



*Members of INFLA-CARE and Scientific Advisory Board (SAB) in Athens meeting 2011, from left Jiri Bartek (University of Olomouc, Czech Republic), Curt Harris (SAB, NIH, USA), project coordinator Aris Eliopoulos (IMBB, Greece), Vishva Dixit (SAB, Genetech, USA), Constantinos Papadakis (University of Crete, Greece), Manolis Pasparakis (University of Cologne, Germany).*

## **INFLA-CARE Summer School**

The 4<sup>th</sup> annual meeting in September will be followed by a 2<sup>nd</sup> Summer School on “*Inflammation, Cancer and Novel Therapeutics*”, which will be held in conjunction with 2 other EC-funded programmes (*TransPOT* – Building Excellence in Translational Medical Research and *TACIT* - Targeted Oligonucleotides in Immunotherapy) to increase the dissemination of knowledge of the meeting. We hope this event will be as stimulating and enjoyable for our participants as our previous summer school in 2010 was. In addition to consortium members, our Summer School speakers include Christoph Becker (Germany), Vincenzo Bronte (Italy), Vishva Dixit (USA), Curt Harris (USA), Poul Sorensen (Canada), Philip Tschlis (USA) and Karin de Visser (Netherlands). Information on how to register for this event is now available at [www.inflacare2012.gr](http://www.inflacare2012.gr)



*Members of INFLA-CARE attending the 3<sup>rd</sup> Annual Meeting in Athens, September 2011.*

Institute of Molecular Biology & Biotechnology  
and University of Crete Medical School

# 2<sup>nd</sup> Inflammation, Cancer and Novel Therapeutics Conference & Summer School

## 24-27 September 2012

Ikaros Beach Resort & Spa  
Crete, Greece

### Topics:

- Molecular mechanisms of carcinogenesis
- Cytokines, senescence and cancer
- The tumor microenvironment
- Signaling pathways in inflammation and cancer
- Lung, liver & gut inflammatory diseases
- In silico and transgenic models
- Novel therapeutic modalities
- Novel therapeutic targets

[www.inflacare2012.gr](http://www.inflacare2012.gr)

**Abstract Deadline: August 20<sup>th</sup> 2012**

Conference Secretary: Georgia Houlaki ([info@inflacare2012.gr](mailto:info@inflacare2012.gr))

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Targeted Oligonucleotide Carriers for Immuno-Therapy (TACIT)  
Enhancing the Translational Research Potential of the University of Crete Medical School (TransPOT)



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