



JOINT EVENT

5th World Conference on **Climate Change**

&

16th Annual Meeting on

Environmental Toxicology and Biological Systems

October 04-06, 2018

London, UK

Keynote Forum

Day 1

Climate Change 2018 & Global ENVITOX 2018

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16th Annual Meeting onOctober 04-06, 2018
London, UK**Environmental Toxicology and Biological Systems****Edwin John Routledge***Brunel University London, UK***Towards a sustainable chemical future**

Since the start of the industrial revolution, society has become increasingly reliant on the use of chemicals, including pesticides, pharmaceuticals, plasticizers and personal care products, to name a few. In 2016, European chemical sales alone were valued at 507 billion Euros, with 80,000 chemicals reported to be in common use worldwide. Alongside the many benefits of chemicals to society, concerns about the impacts of certain chemicals to both human and wildlife health, including the so-called 'endocrine disrupting chemicals' is a topic of increasing concern. Since the term 'endocrine disruptor' was coined in 1991, extensive research into the effects of various chemicals, and chemical mixtures, on human and wildlife health has been conducted globally. More than 1,300 studies have suggested connections between endocrine-disrupting chemical (EDC) exposure and serious health conditions such as infertility, diabetes, obesity, hormone-related cancers and neurological disorders in humans. The range of endocrine targets captured by regulatory tests is expanding rapidly, and new mechanistic insights, such as epigenetic mechanisms of chemical-induced disease, continue to challenge the regulatory frameworks designed to protect society and the environment. Difficulties still exist in balancing the trade-offs between the benefits of chemicals to society at point of use with the burden of proof needed to demonstrate the adverse consequences of the same chemicals once they are allowed to disperse in the environment. When dealing with such complexity, is it possible to achieve a vision of a sustainable society where chemicals are managed carefully throughout their lifecycle and where people benefit from their use and thrive within nature's limits? What strategies and insights can sustainability science offer to help society balance the Tox-Eco system?

Recent Publications

1. Kaur S, Jobling S, Jones CS, Noble LR, Routledge EJ, Lockyer AE (2015) The Nuclear Receptors of *Biomphalaria glabrata* and *Lottia gigantea*: Implications for Developing New Model Organisms. *PLOS One* 10(4): UNSP e0121259.
2. Bannister R, Beresford N, Granger DW, Pounds NA, Rand-Weaver M, White R, Jobling S, Routledge EJ (2013) No substantial changes in estrogen receptor and estrogen-related receptor orthologue gene transcription in *Marisa cornuarietis* exposed to estrogenic chemicals. *Aquatic Toxicology* 140: 19-26.
3. Routledge EJ, White R, Parker MG, Sumpter JP (2000) Differential effects of xenoestrogens on coactivator recruitment by estrogen receptor (ER) alpha and ER beta. *Journal of Biological Chemistry* 275(46): 35986-35993.
4. Routledge EJ, Parker J, Odum J, Ashby J, Sumpter JP (1998) Some alkyl hydroxy benzoate preservatives (parabens) are estrogenic. *Toxicology and Applied Pharmacology* 153(1): 12-19.
5. Routledge EJ & Sumpter JP (1996) Estrogenic activity of surfactants and some of their degradation products assessed using a recombinant yeast screen. *Environmental Toxicology and Chemistry* 15(3): 241-248.

Biography

Edwin John Routledge is an Environmental Scientist whose research is concerned with understanding the effects of environmental chemicals (particularly endocrine disrupting chemicals) on aquatic wildlife. His research interest is broadly in the field of water quality. It started with investigations into endocrine disrupting chemicals and their effects on fish and amphibians, and more recently includes the effects of EDCs on molluscs. Current research (mostly unpublished) is concerned with new and emerging threats, including chemicals that impact on the retinoid system, and how chemical exposures might alter disease transmission in parasite-host interactions.

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London, UK**Environmental Toxicology and Biological Systems****Manuela Marcoli**

University of Genova, Italy

Functional neuron-specific endpoints for *in vitro* neurotoxicity testing

Statement of the Problem: In accordance with 3Rs, alternative models are required to replace standard neurotoxicity testing. High-content, high-throughput tools are needed considering specific features of nervous system (NS) functioning to identify neurotoxic vs. cytotoxic effects. By considering intercellular communication through transmitters and transmitter sensors (receptors), and collective behavior of neuron network as relevant NS functional features, the purpose of this study is to develop tools providing neuron-specific endpoints.

Methodology & Theoretical Orientation: A multi-disciplinary electrophysiological, neurochemical and immunocytochemical approach, combining electrical activity recording of neuron network (on engineered micro-electrode arrays (MEAs) equipped with 60 electrodes onto which cerebrocortical neurons were cultured; data analysis through a home-made software and measurement of transmitter release was used to assess network maturation and to detect effectiveness of neuroactive/neurotoxic substances.

Findings: During network development, maturation of glutamatergic/GABAergic neuron networks, target for relevant neurotoxicity mechanisms (excitotoxicity) and drugs classes, was observed. In mature networks, synaptic connectivity was related to activation of glutamatergic pathways, and the system behaved as a sensitive sensor of glutamatergic transmission functioning. Activation or blockade of NMDA/AMPA receptors, or blockade of glutamate transporters, induced firing and bursting activity variations related to the effects on transmitter release. Also, the network sensed the fine transmission variations involved in synapse plasticity: the collective network behavior and glutamate release were controlled by NMDA-dependent NO-cGMP pathway, as indicated by its pharmacological manipulation (NO synthase/guanylyl cyclase inhibitors, NO donors/8Br-cGMP). By presenting examples of network activity modulation by neuroactive substances (glutamate/GABA receptor agonists/antagonists) and by known neurotoxicants (e.g., domoic acid, chlorpyrifos oxon), and ineffectiveness of molecules not exhibiting acute neurotoxic effects, we report evidence that MEAs-coupled neuron networks can represent an integrated approach for neurotoxicity testing based on functional neuron-specific endpoints. They might provide an effective *in vitro* alternative tool for evaluating substance neurotoxicity, also providing a mechanistic approach.

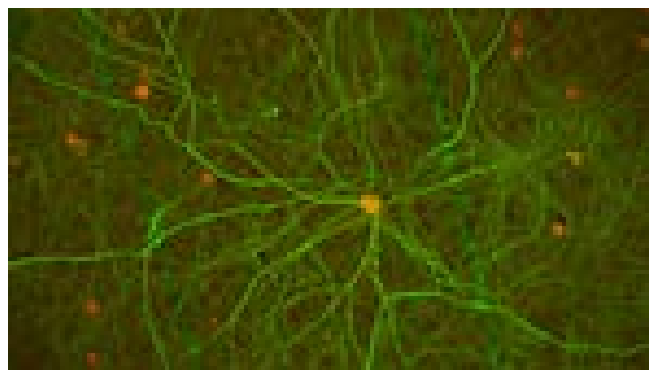
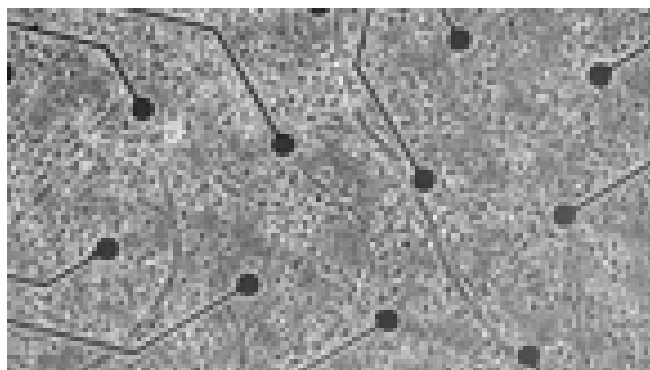


Figure 1: Neuron network on MEAs; primary rat cerebrocortical neuron cultures from E19, 24 DIV. The network on microelectrode arrays is shown. Immunocytochemistry for MAP2 (green) and NeuN (red).

Environmental Toxicology and Biological Systems

Recent Publications

1. Frega M, Pasquale V, Tedesco M, Marcoli M, Contestabile A, et al. (2012) Cortical cultures coupled to micro-electrode arrays: a novel approach to perform in vitro excitotoxicity testing. *Neurotoxicol Teratol* 34:116–127.
2. Marcoli M, Agnati L F, Benedetti F, Genedani S, Guidolin D, et al. (2015) On the role of the extracellular space on the holistic behaviour of the brain. *Rev Neurosci* 26(5):489–506.
3. Fuxe J, Agnati L F, Marcoli M and Borroto-Escuela D (2015) Volume transmission in central dopamine and noradrenaline neurons and its astroglial target. *Neurochem Res* 40(12):2600–14.
4. Cervetto C, Vergani L, Passalacqua M, Ragazzoni M, Venturini A, et al. (2016) Astrocyte-dependent vulnerability to excitotoxicity in spermine oxidase overexpressing mouse. *Neuromolecular Med* 18:50–68.
5. Pietropaoli S, Leonetti A, Cervetto C, Venturini A, Mastrantonio R, et al. (2018) Glutamate excitotoxicity linked to spermine oxidase overexpression. *Mol Neurobiol*. 55(9):7259–7270.

Biography

Manuela Marcoli has more than 20 years' experience in studying neurotransmission in the central and peripheral nervous system. She has completed her MD and PhD in Clinical Pharmacology from Pavia University, Italy. She is a Professor of Pharmacology at the University of Genova, Italy. Main research fields are glutamatergic transmission: ionotropic/metabotropic receptors and release of neuro- and glio-transmitters in physiological conditions and in pathological animal models; network activity and transmitter receptors in neuron-astrocyte networks on multi electrode arrays: effects of neuroactive substances and neurotoxicants. She has over 85 publications in peer-reviewed journals and has been serving as a Reviewer of reputed journals.

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JOINT EVENT

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&

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London, UK**Environmental Toxicology and Biological Systems****Simon A Morley**

British Antarctic Survey, UK

Antarctic marine biodiversity and climate change

Human culture and food security rely on the ecosystem services provided by historic patterns of biodiversity. We therefore need to understand the factors that determine where species can and cannot live, and the impact of both natural and anthropogenic variation. Such predictions require an understanding of the mechanisms underlying species range limits, and how they are linked to climate. The Southern Ocean offers a “natural laboratory” for testing the evolutionary and physiological capacity of species in response to their environment. Its isolation has resulted in high levels of endemism and the lack of indigenous humans means that the environment is close to pristine. It is a constantly cold ocean but with large seasonal variation in light levels, primary productivity and pH. Animals living in the Southern Ocean have several physiological adaptations for life in the cold, including natural antifreeze, increased mitochondrial densities and the ability to grow to a large size. Life in the extreme cold has also resulted in a reduced ability to cope with warming. The activity limits for limpets and clams are only 1 to 2°C above current maximum summer temperatures. Comparisons of long-term oceanographic and reproductive data-sets have shown that one of the strongest signals affecting inter-annual variability in reproduction is El Niño, which causes dramatic changes in the coastal system. In addition to this understanding, the Western Antarctic Peninsula has been one of the fastest warming regions, resulting in massive changes in the cryosphere. The reduction in the duration of winter sea ice, an increase in energy transfer from the atmosphere and the increase in iceberg scour has resulted in dramatic changes in benthic communities. Findings from the Antarctic have taught us much about the evolution of physiological capacity and the evolution of marine communities across latitudes.

Recent Publications

1. Ashton G V, Morley S A, Barnes D K A, Clark M S and Peck L S (2017) Warming by 1°C drives species and assemblage level responses in Antarctica’s marine shallows. *Current Biology* 27(17):2698–2705.
2. Watson S A, Morley S A and Peck L S (2017) Latitudinal trends in shell production cost from the tropics to the poles *Science Advances* 3(9):e1701362.
3. Morley S A, Nguyen K D, Peck L S, Lai C-H and Tan K S (2017) Can acclimation of thermal tolerance, in adults and across generations, act as a buffer against climate change in tropical marine ectotherms? *J Therm. Biol.* 68:195–199.
4. Morley S A, Suckling C S, Clark M S, Cross E L and Peck L S (2016) Long term effects of altered pH and temperature on the feeding energetics of the Antarctic sea urchin, *Sterechinus neumayeri*. *Biodiversity* 17:34–45.
5. Morley S A Chien-Hsian L, Clarke A, Tan K S, Thorne M A S and Peck L S (2014) Limpet feeding rate and the consistency of physiological response to temperature. *J Comp Physiol.* 184:563–570.

**Biography**

Simon A Morley’s research has a latitudinal focus on understanding the mechanisms that determine species tolerance and plasticity. He is a trained Physiologist completing a PhD with the University of Liverpool in 1998 before a Postdoctoral position at the University of Bangor before he joined the British Antarctic Survey as a Fisheries Ecologist, and spent two years based at King Edward Point at the Island of South Georgia.

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16th Annual Meeting on

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Environmental Toxicology and Biological Systems



Carolyn (Tally) Palmer

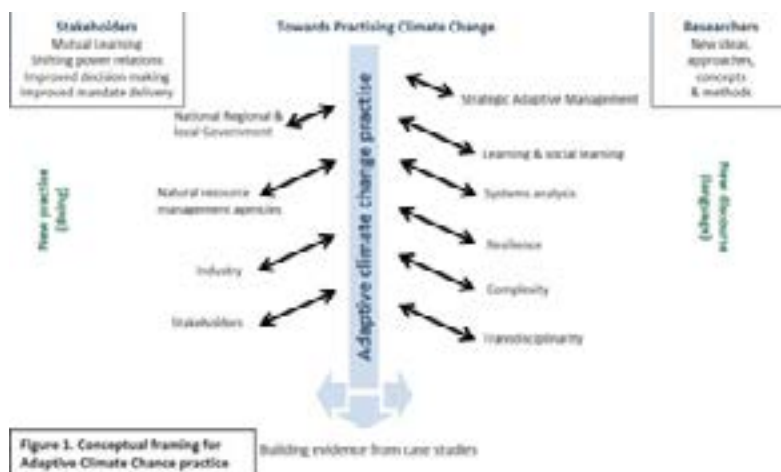
Rhodes University, South Africa

Too slow and too difficult? participatory governance as a lever for climate change adaptation

Statement of the Problem: Interventions for development, sustainability, and/or climate change adaptation have a history of ambiguous outcomes and outright failures. How can interventions, and especially those that involve government, research and stakeholders, including local residents, result in sustainable outcomes that persist beyond the intervention, and move towards climate change behavior-change in the practice of all participants?

Methodology & Theoretical Orientation: The underpinning methodology is transdisciplinary (TD). Critical realism provides a theoretical foundation for discerning causal mechanisms in complex systems using the full range of disciplinary enquiry. The concept of complex social-ecological systems (CSES) provides a lens to forefront the role adaptation and feed-back. Expansive learning provides the mechanisms to guide processes of co-learning and the co-development of knowledge. Strategic adaptive management provides practical on-the-ground steps for stakeholders to participate in an adaptation process. The governance system in each particular CSES provides the contextual possibility of a process that will persist. Participatory governance brings the vitality and relevance of civil society. Eight case studies to probe the challenging question of whether painstaking on-the-ground trust-building; activating participatory governance processes; and engaging in reflexive praxis, can catalyze change towards climate change adaptation, specifically focusing on water scarcity.

Conclusion & Significance: The selected approach is slow, with many pitfalls. There are not many examples of unequivocal success. However, we can demonstrate learning, begin to understand failure more deeply, and most importantly share “narratives of hope”. Pace of progress and the difficulty of persevering. These “narratives of hope” are the landmarks to encourage perseverance until a bigger body of evidence emerges and principles of practice are refined. We have enough examples of participatory governance being a key lever for ongoing change towards climate change adaptation to suggest it is worth persevering. The approach is easy to criticize – especially in terms of the pace of progress and the difficulty of persevering with these processes. These “narratives of hope” are the landmarks to encourage perseverance until a bigger body of evidence emerges and principles of practice are refined.



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Recent Publications

1. Palmer C G, Biggs R and Cumming G S (2015) Applied research for enhancing human well-being and environmental stewardship: using complexity thinking in Southern Africa. *Ecology and Society* 20(1):53.
2. Lang D J, Wiek A, Bermann M, Stauffacher M, Martens P, et al. (2012) Transdisciplinary research in sustainability science: practice, principles, and challenges. *Sustainability Science* 7(5):25–43.
3. Folke C (2006) Resilience: the emergence of a perspective for social-ecological systems analyses. *Global Environmental Change* 16(3):253–267.
4. Cilliers P (2000) What can we learn from a theory of complexity? *Emergence* 2(1):23-33.

Biography

Carolyn (Tally) Palmer has a research trajectory from aquatic ecology and environmental water quality, together with water law and policy development, to a commitment to the transformative capacity of engaged, transdisciplinary action research praxis, based on a conceptual framing of complex social-ecological systems. Her concept of Adaptive Integrated Water Resource Management includes the recognition that participatory governance – people at the interface of knowledge production, practice and politics creates a sustainability platform and pathway that can be the foundation of local to at least national scale climate-change adaptation. At the interface of sustainability science, policy, and practice it is practice that most often fails. Carolyn brings a coherent set of transdisciplinary case studies from across South Africa to argue that participatory governance can be a key lever to embed climate change adaptation practice, making the most of linked research and development interventions.

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&

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Environmental Toxicology and Biological Systems



Volker M Arlt

King's College London, UK

Modelling mutational signatures of environmental carcinogens in cultured human cells

Whole genome sequencing (WGS) of human tumors has revealed distinct patterns of mutation that hint at the causative origins of cancer. The Catalogue of Somatic Mutations in Cancer (COSMIC) is a global resource for information on somatic mutations in human cancer and currently lists 30 distinct mutational signatures. Some signatures are correlated with known environmental exposures, but the causative origins of many signatures remain unknown. We have developed an experimental approach using human induced pluripotent stem (iPS) cells to define mutational signatures of environmental carcinogens by WGS. Treatment conditions (e.g. concentration) for WGS were optimized by assessing cytotoxicity, DNA damage response signaling and the formation of premutagenic DNA adducts. After WGS, a ubiquitous background mutational signature was extracted in all clones showing similarities with COSMIC Signature 18 which has been reported in other cultured human cells. Specific signatures were identified in human iPS cells, following exposure to benzo[a]pyrene (BaP), simulated sunlight aristolochic acid I (AAI) and aflatoxin B1 (AFB1), revealing characteristic mutation pattern for each carcinogen that were highly similar to COSMIC signatures of mutations found in tumors of individuals who were exposed to the agent of interest: predominantly G to T mutations for BaP were linked to COSMIC Signature 4; C to T for simulated sunlight was linked to COSMIC Signature 7; A to T for AAI was linked to COSMIC Signature 22; and G to T for AFB1 was linked to COSMIC Signature 24. Thus, human cell-based systems and WGS can be used to study the genome as a record of environmental exposure.

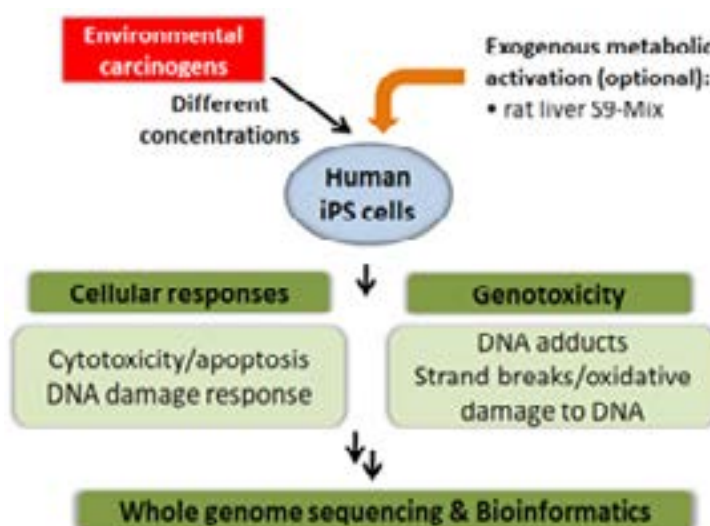


Figure 1: Experimental design for modelling the mutational signatures of DNA damaging agents in human induced pluripotent stem (iPS) cells by whole genome sequencing.

Environmental Toxicology and Biological Systems

Recent Publications

1. Long A S, Wills J W, Krolak D, Guo M, Dertinger S D, et al. (2018) Benchmark dose analyses of multiple genetic toxicity endpoints permit robust, cross-tissue comparisons of MutaMouse responses to orally delivered benzo[a]pyrene. *Arch. Toxicol.* 92(2):967–982.
2. White P A, Douglas G R, Phillips D H and Arlt V M (2017) Quantitative relationships between lacZ mutant frequency and DNA adduct frequency in Muta™Mouse tissues and cultured cells exposed to 3-nitrobenzanthrone. *Mutagenesis* 32(2):299–312.
3. Kucab J E, Zwart E P, van Steeg H, Luijten M, Schmeiser H H, et al. (2016) TP53 and lacZ mutagenesis induced by 3-nitrobenzanthrone in Xpa-deficient human TP53 knock-in mouse embryo fibroblasts. *DNA Repair* 39:21–33.
4. Nik-Zainal S, Kucab J E, Morganella S, Glodzik D, Alexandrov L B, et al. (2015) The genome as a record of environmental exposure. *Mutagenesis* 30(6):763–70.
5. Kucab J E, van Steeg H, Luijten M, Schmeiser H H, White PA, et al. (2015) TP53 mutations induced by BPDE in Xpa-WT and Xpa-Null human TP53 knock-in (Hupki) mouse embryo fibroblasts. *Mutat. Res.* 773:48–62.

Biography

Volker M Arlt has an international profile of research in Environmental Carcinogenesis and Toxicology evidenced by over 180 articles published in high-ranked international journals within the field of research. His expertise is firmly rooted in Molecular Carcinogenesis as well as Genetic and Environmental Toxicology. He is Senior Lecturer in Environmental and Genetic Toxicology at King's College London and based at the Department of Analytical, Environmental and Forensic Sciences within the School of Population Health & Environmental Sciences. He also belongs to the MRC-PHE Centre for Environmental & Health. He is a European Registered Toxicologist.

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&

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London, UK**Environmental Toxicology and Biological Systems****Jean-Claude Gascard**

French National Center for Scientific Research, France

Arctic sea ice decline over the past 40 years

The Arctic sea ice extent and thickness has declined by 50% over the past 40 years and consequently the ice volume which is a by-product of both Arctic sea ice extent and thickness has declined by 75% during summer. This is a huge change among all the elements contributing to Earth's climate change. To understand and to explain this situation and to find out about its origin, it is essential to look at winter, in addition to summer conditions. Based on freezing degree days (FDD) accumulating all over the freezing season each year, starting in September and ending in May the following year, we are able to demonstrate that the decline in Arctic sea ice over the past 40 years is largely due to milder winters and the lack of freezing in winter. Sea ice newly formed during each winter is not able to balance the Arctic sea ice melting during the summer season even if there are more new ice formed due to a larger ice free ocean undergoing freezing every year. During the past two years, we registered a sharp drop of more than 10 cm of sea ice thickness compared to the previous year indicating the phenomenon we just described as accelerating. This is mainly due to warm air masses and warm oceanic waters advected from the South to the Arctic Ocean. Based on these results, it is highly probable and almost inevitable that Arctic sea ice will disappear in summer within the coming 10 years with large consequences for the Earth's climate in the Northern Hemisphere and also globally. We are already experiencing frequent cold air outbreaks at mid latitudes as well as heat waves propagating up to the North Pole as described recently (February 25, 2018) by the weather previsionist (Etienne Kapikian) from Meteo-France.

Recent Publications

1. Gascard J-C, Riemann-Campe K, Gerdes R, Schyberg H, Randriamampianina R, et al. (2018) Future sea ice conditions and weather forecasts in the Arctic: implications for Arctic shipping. *AMBIO* 46:355–367.
2. Gascard J-C, et al. (2015) General introduction to the DAMOCLES special issue. *Atmospheric Chemistry and Physics* 15:5377–5379.
3. Bourgain P, Gascard J-C, Shi J and Zhao J (2013) Large scale temperature and salinity changes in the upper Canadian Basin of the Arctic Ocean at a time of a drastic Arctic oscillation inversion. *Ocean Sciences* 9:447–460.
4. Bourgain P and Gascard J-C (2012) The Atlantic and Pacific waters variability in the Arctic Ocean from 1997 to 2008. *Geophysical Research Letters* 39.
5. Bourgain P and Gascard J-C (2011) The Arctic Ocean halocline and its interannual variability from 1997 to 2008. *Deep Sea Research* I 58:745–756.

Biography

Jean-Claude Gascard is a Physical Oceanographer specializing in Deep Ocean Convection and Polar Oceanography. He started his observations in the Mediterranean Sea in the 1970s leading to his Doctorate Degree in 1977, then in the Labrador Sea and in the Greenland Sea in the 90s when he published a paper in *Nature* about Sub-mesoscale Coherent Vortex (SCV) generated during deep ocean convection. This is a major element of the thermohaline ocean circulation mechanism often called the great conveyor belt. His first Arctic expedition was in 1983–1984 during the MIZEX experiment in Fram Strait. He led large European projects in the Arctic during the International Polar Year: the DAMOCLES project from 2005 to 2010 and more recently the ACCESS project (2011-2015) a multidisciplinary Arctic project for understanding the impacts of the Arctic climate change on the economy and the society. He has published more than 100 papers and edited four books.

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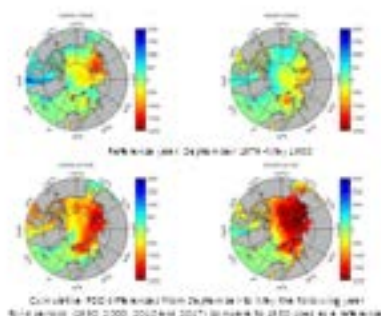
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London, UK**Environmental Toxicology and Biological Systems****Sujata Law***Calcutta School of Tropical Medicine, India***Agricultural pesticide induced bone marrow aplastic anaemia and the hedgehog signaling scenario**

Multiple health hazards and fatalities from the widespread use of pesticides have been reported by the WHO. Developing countries primarily dependent on agriculture for their economies such as India, Bangladesh and Thailand are especially reliant on these chemicals. Consequentially, public health has been on a decline and there is a lacuna of knowledge about the effect of pesticide exposure on bone marrow haematopoietic system. The on-field scenario was mimicked in murine model to explore the consequences of chronic pesticide exposure. In the present work, we have developed an agricultural pesticide formulation (fungicide, organophosphate and pyrethroid) induced bone marrow aplasia mouse model to recapitulate the human aplastic anemia like condition in the laboratory to study the aplastic hematopoietic microenvironment in the light of Hh-GLI signaling pathway. Our study has unfolded the fact that chronic pesticide exposure caused downregulation of intrasignaling feedback of PATCH1 and GLI1 by inhibiting the SMO internalization and upregulating downstream negative regulators SU(FU), PKC- δ and β TrCP. Upregulation of negative regulators not only hampers the execution of the hedgehog signaling but also cripples the autocrine-paracrine crosstalk in between bone marrow primitive compartment and stromal compartment. Simultaneously, individual pesticide versus hedgehog signaling study revealed that hexaconazole disrupted hematopoietic hedgehog signaling activation by inhibiting SMO and facilitating PKC- δ expression. Contrarily, chloropyrifos increased the cytoplasmic sequestration and degradation of GLI1 by upregulating SU(FU) and β TrCP sequentially. Whereas, cypermethrin mediated antagonization of the hedgehog signaling was circumvented by non-canonical activation of GLI1. However, such marrow degenerative condition can be compensated by the recombinant sonic hedgehog. We can conclude that pesticide exposure induced bone marrow aplasia is the direct manifestation of downregulated hedgehog signaling in the bone marrow microenvironment.

**Biography**

Sujata Law did her PhD in Stem Cell Biology from the University of Calcutta and Postdoctoral studies in the field of Signal Transduction from Bose Institute, Kolkata. She is in the Faculty of Stem Cell Biology in the Department of Biochemistry & Medical Biotechnology at Calcutta School of Tropical Medicine a hundred years old government institution Kolkata, India. She has teaching experience in the field of Physiology, Signal Transduction, Cell Culture and Tissue Engineering, Haematology, Stem Cells, Cellular Immunology, Cell Biology, and aspects of Molecular Biology and Biotechnology at postgraduate level and received many research projects as Principal Investigator from various government scientific organizations like CSIR, ICMR, DST, DBT, etc. She has 57 publications in various international and national reputed journals and has guided many PhD students and delivered invited talks in India and abroad.

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