News & Views

Iran Welcomes Alternatives Outreach

InterNICHE was present at the 17th Iranian Veterinary Congress, in Tehran, as part of an outreach project that also included visits to Uzbekistan and Kyrgyzstan.

The presentation on humane education and alternatives at the congress in Tehran was complemented by a stall co-organised by InterNICHE and the Iranian Anti-Vivisection Association (IAVA). A range of alternatives, including software, models, mannekins and simulators were presented, and generated positive feedback from veterinary teachers and students.

A meeting with zoologists at the Marine Sciences University was held, and talks to over 100 people were given at two branches of the Islamic Azad University (the Faculty of Veterinary Medicine in Garmsar and the Science and Research Branch in Shahriar), organised by IAVA Director, Dr Ramak Roshanaie. Veterinarian Dr Shahabeddin Safi presented the case for alternatives in research and testing, and Nick Jukes (InterNICHE) explored the range and quality of alternatives in education and training. Demonstrations of innovative learning tools within anatomy, physiology, pharmacology, clinical skills and surgery, were given. For many teachers and students, this was their first significant exposure to alternatives, and the first time that animal experiments had been comprehensively challenged. Student interest was very high, reflecting widespread discomfort with harmful animal use, and many teachers recognised the pedagogical, ethical and economic advantages of alternatives.

At another meeting, the Dean of the Veterinary Faculty at Tehran University was very positive, acknowledging the positive role that alternatives can play within education, and placing their gradual implementation within the process of reform. Iranian campaigners saw this as a very positive response.

A number of students offered to help with the promotion of alternatives, and a team of student translators was established to help translate the new InterNICHE website into Farsi. A meeting with students from different universities was held, to establish a student alternatives group, and a number of meetings with IAVA campaigners also took place. Such meetings are very important, particularly since Iranian censorship and international sanctions isolate the country and its people from many international connections. In September 2012, IAVA was given the Brown Bear Award by Iran Animal Rights Watch, for being the most active animal rights group in Iran. Campaigners are aware of the multiple positive impact — in terms of pedagogics, ethics and empowerment — of promoting and implementing change and establishing humane education.

Although non-animal learning tools can bring about significant replacement in education and training, in veterinary medicine there is a genuine need for access to animal tissues. Some universities kill animals for their cadavers, and it is wrongly assumed that, if animal tissues are necessary, that there is no other choice. The provision of ethically-sourced animal cadavers through Body Donation Programmes offers a creative, ethical solution that is increasingly being explored by universities.

For many alternative methods, the sanctions were identified as a barrier to their import and subsequent implementation. The local production of alternatives was recognised as a potential solution. Another area of interest from teachers was reflected in requests that InterNICHE and IAVA should organise a workshop on plastination. This method of dehydrating tissue and employing silicone and other materials to preserve specimens, can produce durable models that are alternatives to dissection. Working with this specific interest indicated by the teachers, will also provide an opportunity to open the door to the broader field of alternatives.[1]

[1] Anon. (2012). *Alternatives outreach in Iran a success*. [InterNICHE, 03.12.12]. Available at: http://www.interniche.org/en/news/alternatives-outreach-iran (Accessed 13.10.12).

InterNICHE Database

The InterNICHE Studies Database, which provides material on humane education and training, is now offering a collection of selected full-content pdf files, including selected *ATLA* papers, for public download.

The Studies Database is a free-access information resource that provides studies on various themes, such as technological innovation, experience of implementation, assessment, comparative studies, and training.[1] It aims to provide relevant information on, for example, teaching objectives, the hidden curriculum and objections to alternative physiology classes, and

microsurgical training. It currently contains more than 800 studies, and over 1600 more are planned for inclusion. Studies addressing training in humane research and testing, such as toxicology *in vitro*, are also being added.

The database is available at: http://www.interniche.org/studies

[1] Anon. (2012). *InterNICHE studies database*. Available at: http://www.interniche.org/studies (Accessed 13.10.12).

Bio-bank for Research in Saudia Arabia

The King Abdullah International Medical Research Center (KAIMRC), in Saudi Arabia, plans to create a bio-bank with about 200,000 human samples, for use in studies on diseases widespread in the Kingdom.[1]

The bank will collect blood, saliva, urine and tissue samples from volunteer patients at medical institutions run by the National Guard Health Affairs. In addition, data on the individuals' lifestyle and physical aspects will be regularly collected and stored for future analysis. The diseases covered include: diabetes, cancer, coronary artery disease, hepatitis, obesity, bronchial asthma, chronic renal impairment and failure, and stroke.

As Saudi Arabia has a relatively large number of consanguineous families, these samples are particularly important for research on diseases with a genetic component. The bio-bank is part of an ongoing effort to improve healthcare services in Saudi Arabia — it will be used to educate people on risk factors for certain diseases, and to develop new diagnostic and therapeutic approaches.

Another KAIMRC bank, the Umbilical Cord Blood Bank, will store umbilical cord blood, which can be used for stem cell research and to help patients who need cord blood stem cell transplantation.

[1] Yahia, M. (2012). *Saudi bio-bank to shed light on common diseases in the Kingdom*. [Nature Middle East, 02.12.12]. Available at: http://blogs.nature.com/houseofwisdom/2012/10/saudi-bio-bank-to-shed-light-on-common-diseases-in-the-kingdom.html? WT.ec_id=NMIDDLEEAST-20121004 (Accessed 10.10.12).

Calls for Improved Reporting on Animal Studies

A workshop sponsored by the National Institutes of Health (NIH) National Institute of Neurological Disorders and Stroke (NINDS) has produced a set of recommendations to improve the design and reporting of animal studies.[1] The overall aim is to speed up the development of promising therapies by making animal studies easier to interpret. According to NINDS Director, Dr Story C. Landis, "Our goal is to ensure that preclinical animal studies are reported in sufficient detail, so that funding agencies, scientific journals and the broader scientific community can adequately review the research and decide how to move forward."

The workshop recommendations, which have been published in *Nature*, apply to preclinical animal studies, and state that they should include details on four key aspects of research methodology: randomisation, blinding, sample size estimation, and data handling. According to the recommendations, preclinical studies testing hypotheses about potential treatments should be designed with the same rigor as clinical studies.

The workshop brought together NINDS representatives, patient advocates, and scientists from academia and industry. Editors from selected scientific journals were also present.

[1] Stimson, D. (2012). *NIH–sponsored workshop calls for more detailed reporting in animal studies*. [NIH News, 10.10.12]. Available at: http://www.nih.gov/news/health/oct2012/ninds-10.htm (Accessed 10.10.12).

Alzheimer's Disease

A computational intelligence approach, which used an ensemble of Bayesian classifiers, has been employed to search for relevant genes and gene dependency networks in Alzheimer's disease (AD). The team used machine learning and data mining techniques to compare gene expression levels in two regions of the hippocampus — the dentate gyrus (DG), where AD appears to have no effect, and the entorhinal cortex (EC), which is severely affected.[1]

The study was conducted from two perspectives.[2] First, the expression profiles of EC samples of AD patients and control subjects were compared. Then, the ensemble approach was used to study four types of samples: DG and EC samples from both patients and controls. The analysis identified key metabolic mechanisms that were already known to be involved in AD, such as the deregulation of the *DEC1* and *BTRC* genes that help to regulate the molecular clock controlling the body's circadian rhythm. In fact, in AD, the body loses its circadian reference, leading to sleepless periods that increase beta amyloid levels. The *S100A10* gene, which plays an

important role in serotonin signalling, was also found to be deregulated and differentially expressed in the DG and EC samples. In fact, recent findings have suggested that S100A10 could be used as a new early biomarker of AD.

[1]Facultad de Informática de la Universidad Politécnica de Madrid (2012). *Computational intelligence opens up new avenues in Alzheimer's research*. [AlphaGalileo Foundation, 09.10.12]. Available at: http://www.alphagalileo.org/ViewItem.aspx?ItemId=124757&CultureCode=en (Accessed 10.10.12).

[2]Armañanzas, R., Larrañaga, P. & Bielza, C. (2012). Ensemble transcript interaction networks: A case study on Alzheimer's disease. *Computer Methods & Programs in Biomedicine* **108**, 442–450.

Ex Vivo Tissue Stores Memories

A study has shown that it is possible to store diverse forms of short-term memories, about both temporal sequences and stimulus patterns, directly in isolated brain tissue.

The research, which was published in *Nature Neuroscience*,[1] aimed to elucidate the mechanisms underlying short-term memory *in vitro*, since it has been difficult to link memories with changes in specific neurons or synaptic connections. Isolated rodent brain tissue was used to show that neural circuits in the hippocampus maintained the memory of stimulated input for more than 10 seconds. The information about which pathway was stimulated was evident by the changes in the ongoing activity of brain cells.[2] In addition, it was also possible to generate memories for specific contexts, such as whether a particular pathway was activated alone or as part of a sequence of stimuli to different inputs. According to one of the authors, Robert Hyde, "The type of activity we triggered in isolated brain sections was similar to what other researchers have demonstrated in monkeys taught to perform short-term memory tasks."

[1]Hyde, R.A. & Strowbridge, B.W. (2012). Mnemonic representations of transient stimuli and temporal sequences in the rodent hippocampus *in vitro*. *Nature Neuroscience* **15**, 1430–1438.

[2]Case Western Reserve University (2012). *Researchers create short-term memories* in vitro. [Science Daily, 10.09.12]. Available at: http://www.sciencedaily.com/releases/2012/09/120910143407.htm (Accessed 12.10.12).

Biofabricated Tissues

Researchers in the USA have developed a biofabrication technology called dynamic optical projection stereolithography (DOPsL), that could be used to fabricate, in seconds, microscale 3-D structures out of soft, biocompatible hydrogels.[1]

Some fabrication techniques, such as photolithography and micro-contact printing, are restricted to the generation of relatively simple geometries and 2-D patterns. Stereolithography allows large 3-D objects, such as car parts, to be printed, but a higher resolution would be required to reproduce biological tissues.

This novel technique, which is being developed in the laboratory of Professor Shaochen Chen, with funding from the National Institutes of Health, uses a computer projection system and precisely controlled micromirrors to shine light on a selected area of a solution containing photo-sensitive biopolymers and cells. This photo-induced solidification process forms one layer of solid structure at a time, but in a continuous fashion until the required structure is complete. In the short-term, this technology might be used to fabricate 3-D systems for culturing and studying cells *in vitro*, but the ultimate goal is to be able to print biological tissues for regenerative medicine.[2]

[1]Zhang, A.P., Qu, X., Soman, P., Hribar, K.C., Lee, J.W., Chen, S. & He, S. (2012). Rapid fabrication of complex 3D extracellular microenvironments by dynamic optical projection stereolithography. *Advanced Materials* **24**, 4266–4270.

[2]Anon. (2012). *Nanoengineers can print 3D microstructures in mere seconds*. [UCSD Jacobs, 13.09.12]. Available at: http://www.jacobsschool.ucsd.edu/news/news_releases/release.sfe?id=1259 (Accessed 15.10.12).

Free Database of Drugs Associated with Liver Injury

The National Institutes of Health (NIH) have launched the LiverTox database,[1] a free evidence-based information resource on liver injury associated with drugs and herbal and dietary supplements. The database is aimed at researchers and healthcare professionals who wish to identify basic and clinical research topics and to optimise the diagnosis and control of drug-induced liver injury (DILI).

DILI is a leading cause of acute liver failure. According to Dr Jay Hoofnagle, the major creator of LiverTox, "Because drug-induced liver disease is not a single, common disease, it is very difficult to diagnose, with each drug causing a somewhat different pattern of liver damage". Drugs can damage the liver directly, but DILI can also be a consequence of other effects or caused by an allergic reaction. Pinpointing the source of DILI is the crucial step in the elimination or minimisation of the damage.

LiverTox consists of a searchable database of about 700 prescription and over the counter medications that are available in the USA. Another 300 drugs will be added over the next few years. The database offers: an overview of DILI (including diagnosis); a detailed report of each drug and references with links; and an interactive section where cases can be reported (and which are automatically forwarded to the Food and Drug Administration [FDA]'s MedWatch program).

The content of each section of the database has been reviewed by an outside expert, and the finished website has been reviewed by the FDA and industry experts. Dr Hoofnagle said that, "By integrating data that tends to be scattered across the published literature into a single, readily accessible place, we hope to bring greater focus and interest to the study of drug-induced liver injury, and to guide doctors involved with patient care and ultimately, reduce liver injury and improve the health of people".

LiverTox will be updated regularly, and feedback is welcomed through the website at www.livertox.nih.gov.

[1] Cravedi, K. (2012). *NIH launches free database of drugs associated with liver injury.* [NIH, 12.10.12]. Available at: http://www.nih.gov/news/health/oct2012/niddk-12.htm (Accessed 17.10.12).

Men and Women Respond Differently to Treatment

An Austrian multicentre study with human patients has found that gender can affect the outcome of immunotherapy — women respond much better than men to the treatment of chronic follicular lymphoma with a monoclonal antibody that targets CD20 (rituximab).

Follicular lymphoma is a chronic cancer of the lymphatic glands, which frequently recurs after a temporary remission. Female patients, in general, had been known to have a better prognosis after rituximab treatment. The results of the study, which were published in *Haematologica*,[1] indicate that over the period of treatment with rituximab, serum concentrations in women are approximately 20% higher than in men. In women, saturation of the blood concentration with the antibody was achieved during the fourth cycle of treatment, which is significantly earlier than in men. According to one of the authors of the paper, Dr Ulrich Jäger, future studies will "look at other conditions in which antibodies are used in order to determine whether there is a similar gender-specific effect taking place."[2]

[1] Jäger, U., Fridrik, M., Zeitlinger, M., Heintel, D., Hopfinger, G., Burgstaller, S., Mannhalter, C., Oberaigner, W., Porpaczy, E., Skrabs, C., Einberger, C., Drach, J., Raderer, M., Gaiger, A., Putman, M. & Greil, R. (2012). Rituximab serum concentrations during immuno-chemotherapy of follicular lymphoma correlate with patient gender, bone marrow infiltration and clinical response. *Haematologica* **9**, 1431–1438.

[2] Medical University of Vienna (2012). *Women respond better to the treatment of lymph gland cancer with antibodies than men.* [AlphaGalileo Foundation, 10.10.12]. Available at: http://www.alphagalileo.org/ViewItem.aspx?ItemId=124785&CultureCode=en (Accessed 10.10.12).

Dr Hadwen Trust Grant Applications

The Dr Hadwen Trust is currently inviting new grant applications for research proposals to develop, validate or implement non-animal methods which could contribute to the replacement of animal experiments in medical research.

Grants are available for a maximum of £60,000 *per annum* for up to three years, inclusive of salary, consumables and equipment. Grants for research proposals of shorter duration than three years will be considered pro-rata. Applications for one-year pilot studies are also welcome. As a registered charity, the Dr Hadwen Trust does not award full economic costing, and only provides funds for direct research costs.

The application procedure has two stages — the first is a call for preliminary applications, which must be submitted by Monday, 17 December 2012. Selected preliminary applicants will subsequently be invited to submit full applications in January 2013. For further information, please visit www.drhadwentrust.org. Please note that only non-animal research that has the potential to replace procedures on living animals will be funded.