alamaya
foundation for research in schizophrenia

NEWSLETTER 2013

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NEWS FROM THE FOUNDATON

Between the end of 2012 and the beginning of 2013, several events have brought the Alamaya Foundation to the knowledge of a wider public:

- **LADIES' LUNCH** of Lausanne: twice per year, some 300 women from diverse professional backgrounds gather for a lunch to support a charitable organization. Each lunch is devoted to a cause, which benefits by the funds collected from the ladies and sponsors. The lunch of 8 November 2012 was dedicated to the issue of schizophrenia, and CHF 45,000 have been raised for the Alamaya Foundation – a **wonderful success**, not only on the financial level but also as far visibility is concerned.
- **BRAIN WEEK**:(11-14 March 2013): a booth with information on the Foundation was put at the public's disposal.
- **JOURNÉES DE LA SCHIZOPHRÉNIE**: Alamaya joined in the "Days of Schizophrenia", which took place over the whole French-speaking part of Switzerland in March 2013 – and which celebrated their 10th anniversary. Between the 18th and 21st of March, the Foundation and its mission were made known via an information stall at the CHUV (University Hospital) and at the University of Lausanne.
- Scientific studies supported by the Alamaya Foundation are presented on a regular basis at conferences and congresses in Switzerland and abroad. Between March 2012 and June 2013, Prof. Kim Do Cuénod has been invited to present the results of her research group during **SEMINARS** and scientific **SYMPOSIUMS** in the United States (New York, Philadelphia, San Francisco), in France, Israel, Italy and Sweden; she also gave several **CONFERENCES** in Switzerland, two of which for associations of families and patients living with schizophrenia or other psychiatric disorders, *l'îlot* in Lausanne and *Le Relais* in Geneva. Members of these associations are highly interested in progress achieved on the level of research, on which they set very high hopes.

NEWS FROM RESEARCH

The programme of the Unit for Research in Schizophrenia (URS, Centre for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital) is translational, i.e. it implies a **CONSTANT INTERACTION BETWEEN CLINICAL RESEARCH**, in patients, **AND EXPERIMENTAL RESEARCH**, which uses cell cultures or mice. The main goal consists in uncovering the causes and mechanisms of the disease in order to be able to identify biological markers allowing an **EARLY DIAGNOSIS** as well as therapeutic targets for the development of **NEW TREATMENTS** and **PREVENTIVE MEASURES**. This strategy, which has been successfully applied in somatic medicine (heart, lungs or kidneys for example) for a long time, is relatively new in the field of psychiatry.

The URS has been working for several years with mice in which, as in patients, the gene of the enzyme that synthesizes (produces) glutathione has been modified, so that the level of glutathione stays low and no longer increases normally in response to a higher demand, i.e. when oxidative substances in the human body (free radicals) need to be neutralized.

As a reminder, glutathione is the main protective agent of nerve cells against those substances. As another reminder, schizophrenia results from a combination of genetic factors (among which low glutathione) and environmental factors (various psycho-social stresses) during the development of the brain.

In spring 2013, the team of the URS working on the animal model has published highly significant results.

VULNERABILITY TO STRESS DURING YOUTH AND PROTECTION WITH AN ANTIOXIDANT: the combination of a genetic defect (glutathione deficiency) and an environmental stress in mice has different consequences depending on the age of the animal at the time of the stress: in very young or adolescent mice, it causes a **loss of certain neurons** in the cortex, which are called parvalbumin interneurons; these neurons are **essential for any cognitive or affective performance**. The same cells are deficient in the same brain area in patients. The loss of these neurons is permanent and persists in adult mice. On the other hand, when a stress is applied in the adult animal, it has no deleterious effect on parvalbumin interneurons.

Hence there is a **critical period during youth**, throughout which the brain is particularly sensitive to environmental insults – but this **vulnerability disappears at adulthood**. These findings recall what psychiatrists observe in their patients: they often report major stress situations (loss of a family member, physical or psychological violence, sexual abuse, etc.) during their childhood or adolescence.

Furthermore, the scientific community showed great interest in the following demonstration achieved by the URS team: if an antioxidant (N-acetylcysteine) is administered to the expectant mother and to the young animal exposed to stress, the parvalbumin interneurons stay perfectly normal. This suggests that it could be possible to **protect young at risk subjects with an antioxidant substance** that has no side effects.

The results of these investigations have been published at the beginning of 2013 in the American review ***Biological Psychiatry***, a well-known scientific journal in the field of psychiatry.

PROTECTIVE ROLE OF THE PERINEURONAL NET AGAINST OXIDATIVE STRESS: the URS has also obtained significant results concerning the mechanism involved in the damaging effect of oxidative stress (excess of oxidative substances due to a low glutathione level) on parvalbumin interneurons.
In adults, these neurons are surrounded with a special envelope called "perineuronal net", which develops progressively during the animal's youth until it reaches complete maturity at the age of adulthood. The URS has demonstrated that this envelope, which is known to be partly deficient in the brain of patients suffering from schizophrenia, protects the cell against the deleterious effects of oxidations.

In the young animal, when this protective shell has not yet been formed, the cells suffer in the presence of oxidants, a negative consequence which no longer occurs in the adult animal, when the shell is mature. However, if the perineuronal net is chemically destroyed in adults, parvalbumin interneurons become vulnerable again to oxidative stress, which destroys them.

These observations demonstrate that the perineuronal net and its regulating mechanisms could represent a **new therapeutic target against schizophrenia**. Such a discovery is regarded as a **major progress** for a **better understanding** of the causes of the disease, and an **improved treatment** of patients; it opens up new perspectives for the development of innovative means to protect parvalbumin interneurons.

The results of this study have also been published at the beginning of 2013 in another greatly renowned Amerian journal called ***Proceedings of the National Academy of Science*** (PNAS).

GLUTATHIONE DEFICIENCY AFFECTS THE DEVELOPMENT OF NERVE FIBRES AND MYELIN: another important development deals with nerve fibres, which ensure the connection between the different brain areas and are deficient in patients, and with their protective sheath, called myelin. A doctoral student of the URS has shown that in the animal with low glutathione the formation of myelin is deficient during adolescence. Furthermore, she demonstrated that the cells which are specifically responsible for the formation of myelin are very sensitive to oxidative stress, which hinders their proliferation: the fibres which are in the process of formation will thus have fewer cells at their disposal and the myelin sheath will be deficient.

At the origin of these phenomena, a postdoctoral student of the URS has discovered that an enzyme called "Fyn-Kinase" is increased in animal cells as well as the cells of patients, which paves the way for a **new potential biological marker**.

TRANSLATIONAL INTERACTION IN IMAGING: the imaging of nerve fibres in mice holds specific difficulties given the very small size of their brains. A doctoral student of the URS has developed a method to detect the level of integrity of nerve fibres in the animal model; this has led him to observe the insufficiency of a fascicule of nerve fibres that had never been identified before.
On the basis of this observation in the animal model, a doctor of the Department of Psychiatry (Lausanne University Hospital) has re-examined the brain images of patients, and has discovered anomalies in the same nerve tract. This example highlights once more the **major assets of the translational method** implemented by the URS.

The research programme supported by the Alamaya Foundation continues to gain in **VISIBILITY** and in **CREDIBILITY**. The dissemination of results achieved by the URS is ensured through publications in first rate scientific journals and through presentations at conferences and congresses on the national and the international level, often by invitation. The effort to inform the general public about issues related to schizophrenia is continuously upheld.

On 1 February 2013, professor **KIM DO CUÉNOD**, who heads the Unit for Research in Schizophrenia since its creation in 1999, was appointed **DIRECTOR** of the **CENTRE FOR PSYCHIATRIC NEUROSCIENCE** (Department of Psychiatry, Lausanne University Hospital), taking over from professor Pierre Magistretti.

THANKS TO OUR DONORS, RESEARCH IS TAKING GREAT STEPS FORWARD AND BRINGS BACK HOPE TO PATIENTS AND THEIR FAMILIES.
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Registered Office:	Chemin de la Becque 42, CH – 1814 La Tour-de-Peilz
Secretariat:	Ms Cristina Marich, Le Grand Chemin 63, CH – 1066 Epalinges – Phone +41 (0)21 341 41 03 – Email cmarich@alamaya.net
Bank Details:	Banque Julius Baer & Cie SA, Rue du Grand-Chêne 7-9, CH – 1002 Lausanne
	IBAN: CH 65 0851 5026 0026 6200 3 – BIC: BAERCHZZ – CLEARING: 8515
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