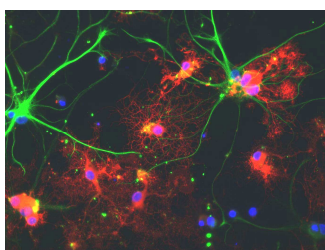


## NEWS FROM THE FOUNDATION

Alamaya is committed to raising the private funds needed to support the scientific programme conducted at the Unit for Research in Schizophrenia (URS, Centre for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital). To this effect, the Foundation works along five main lines:

- It addresses **grant proposals** to funding institutions/foundations in Switzerland and abroad; since several years, Alamaya thus benefits from the generous sponsorship of the *Loterie Romande*, whose contribution allows the financing of various research positions at the URS laboratory.
- It set up a circle of **Friends of the Foundation** open to all people and institutions that are interested in research in schizophrenia, sensitive to the suffering caused by the disease, and willing to donate an annual contribution to the URS programme. The circle was created in 2009 and develops satisfactorily; the first event organized to thank the Foundation's Friends and inform them of recent research outcomes took place in June 2010 (conference and visit of the URS laboratory). Such events, which will focus on various issues, are planned every 12 to 18 months.
- Alamaya strengthened its presence on the **Internet**: the Website [www.alamaya.net](http://www.alamaya.net) is now available in two languages, French and English; a possible translation into German is under consideration.
- **Information counters** are set up during events and meetings in line with the Foundation's sphere of activity (*Semaine du Cerveau, Journées de la Schizophrénie*, etc.);
- **Conferences** are organized for various associations, clubs and other interested organisations.

The above mentioned activities are aimed at building up fundraising assets in particular through enhancing the Foundation's visibility and raising increased awareness among the public as well as private institutions with regard to schizophrenia and other psychiatric diseases which also benefit from research outcomes achieved by the URS (autism, bipolar disorders, major depression).

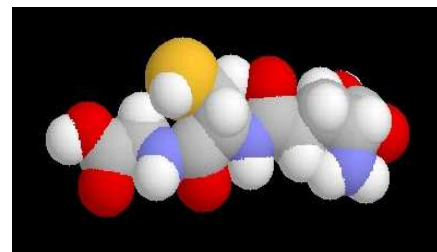


Nerve cells seen  
through a  
microscope

Photo taken from  
an URS study

## NEWS FROM RESEARCH

Research conducted at the URS focuses on the consequences of a **glutathione deficiency** leading to an imbalance between oxidations and reductions ("redox") in the human body, and to an **"oxidative stress"** that is highly damaging for the central nervous system. Glutathione is the main protective agent of nerve cells against aggressions induced by the respiration of oxygen, which generates toxic substances. Insufficient glutathione impedes the normal functioning of **contacts** between nerve cells, and – during the development of the brain – causes anomalies of these **cells** as well as of the **nervous fibres** which ensure their connections. These disturbances are presently considered to be a **risk factor** likely to explain the disorders affecting schizophrenia patients.



Glutathione molecule

### Comparison chronic patients – young patients

The study aimed at young psychotic patients was pursued. The close collaboration with the group of Prof. Philippe Conus (Department of Psychiatry, Lausanne University Hospital), which has been developed over past years, turns out to be very fruitful.

The collection of clinical, psychopathological and neuropsychological data on one hand – as well as genetic, biochemical and imaging data on the other hand – represents a unique and rich source of information concerning each patient, and will contribute to a **better understanding of the disease**. It demonstrated that the large majority of patients show **anomalies of the redox balance**, which the genetic factors that we previously identified can only partly explain. Thus it seems that problems of the redox system **from various origins** generally affect patients suffering from schizophrenia. These findings appear to confirm the hypothesis we proposed in 2009, i.e. that the redox imbalance constitutes a "hub" where a large variety of chain reactions come together, which all end up by generating an oxidative stress.

This oxidative stress, in combination with other pathogenic factors, is likely to cause **anomalies of the nervous system leading to the disease**.

### Clinical trial in early psychosis

**N-acetyl-cysteine (NAC)** is a pharmacological agent that helps **reduce oxidative stress** and **improve the synthesis of glutathione**. In a study we conducted in collaboration with an Australian group, it proved to be beneficial in chronic patients; we therefore set up a **trial with NAC in young patients during their first psychotic episode**.

In the first 24 months of the study, 90 patients (among those corresponding to the study criteria) were clinically well enough to be approached; 31 agreed to participate in the trial and 59 refused; 15 patients completed the 6 month trial and 4 retired. The number of patients who accepted to take part in the study (34.4%) represents a great **success** given the complexity of the study and of the interaction with psychotic individuals. The trial will be continued until 2013 to reach a statistically significant number of participants.

### Animal model with a glutathione deficit

In the field of basic research, the study of our animal model (mice) with a glutathione deficiency is making good progress.

In 2009, we demonstrated that a specific area of the brain – the **hippocampus** – is the site of **alterations of fast spiking inhibitory interneurons** directly involved in a deficit of synchronized neuronal oscillations, **similar to those observed in patients**. Such oscillations play a **key role in the normal functioning of cognitive activities**.

In 2010, the study was expanded to the analysis of another section of the brain which is also involved in schizophrenia: the **anterior cingular cortex**, in the medial part of the frontal lobe.

The animal model showed that **anomalies of inhibitory interneurons** are also present in the anterior cingular cortex; these anomalies are worsened by the impact of an oxidative stress when it occurs during the perinatal or peripubertal development of the animal but not during adulthood. The most remarkable result was achieved through the administration of NAC during the gestation and early stages of the young animal's life: **NAC protects against the anomalies caused by oxidative stress**. These results will be presented at various international meetings and conferences.

### Measure of cerebral metabolites

In collaboration with Professor Rolf Gruetter, Director of the Centre for Biomedical Imaging (CIBM) at the EPFL (Federal School of Technology Lausanne), we studied – in the mouse model with low glutathione – **alterations of cerebral molecules which can be detected and measured by high resolution (14 Tesla) magnetic resonance spectroscopy**. This **highly sophisticated method** holds the advantage of being non-invasive and can be used repeatedly in the same subjects during their development; we also chose it because it is **prime method in translational research**, which requires constant interaction between clinical research (patients) and basic research (cell cultures, mice).

In the young animal, certain **changes** are **very similar to those observed in patients**: in particular, the ratio between two important amino-acids (glutamine / glutamate) increases likewise in the model and in patients. Significantly, **treatment with NAC** during the animal's whole life, from gestation onwards, **restores normal values**. These results will also be presented and published on the international level.



Kim Do Cuénod, Head of the Unit for Research in Schizophrenia, (Centre for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital), was appointed **associate professor** in translational research in psychiatry by the University of Lausanne.

**CONGRATULATIONS!**

**THE ALAMAYA FOUNDATION IS A REGISTERED NOT-FOR-PROFIT ORGANIZATION– DONATIONS ARE TAX DEDUCTIBLE  
MANY THANKS TO ALL THE PEOPLE AND INSTITUTIONS THAT SUPPORT US!**

Avec le soutien de la  
 Loterie Romande

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