An international team of researchers, including CCRN’s Professor Mathew Martin-Iverson and PhD student Zak Millar, has uncovered a new analogue of the designer party drug ‘ecstasy’, which is a promising lead for the treatment of an aggressive form of cancer.

Burkitt’s lymphoma is rare in the developed world, but is the major childhood cancer in sub-Saharan Africa. It affects 25,000 -100,000 people every year, and the incidence is increasing due to higher susceptibility associated with HIV-infection. Burkitt’s lymphoma causes horrific facial tumours that can double in size in one day (see image on left). Effective treatments for Burkitt’s lymphoma are usually too expensive and burdensome for most of those who live with this disease.

The research team noted that the illicit drug methylenedioxyamphetamine (MDMA - see structure below), more commonly known as ‘ecstasy’, kills Burkitt’s lymphoma cells, but only with low potency. Cheap to manufacture, MDMA produces intense euphoria and other effects on the psyche, which has made it a popular recreational drug. Mild euphoria might be a beneficial side-effect in a cancer treatment, the psychological reward of unmodified MDMA might make it liable to abuse and illegal dealing. A major goal of the project was to dissociate the psychoactivity (euphoria and other psychological effects) from the cytotoxicity (the drug’s ability to kill cancer cells).

Associate Professor Matthew Piggott, a medicinal chemist from UWA’s School of Biomedical, Biomolecular and Chemical Sciences, has approached this problem by ‘redesigning’ the drug. By replacing the α-methyl group of MDMA with larger substituents, his team has discovered a compound (UWA-1) that is almost 100 times more potent at killing Burkitt’s lymphoma cells. Mathew Martin-Iverson and Zak Millar have shown that UWA-1 is very unlikely to be psychoactive, and initial tests by other collaborators indicate that it is not neurotoxic.

The research opens the door for the use of MDMA as a lead compound in other indications for which it has shown promising activity; for example, in Parkinson’s disease and post-traumatic stress disorder.

On Friday 3 September, David Lawrence and Francis Mitrou (Curtin University/Telethon Institute for Child Health Research) gave a UWA Psychiatry Research seminar presentation on ‘Smoking and mental illness: implications for public health’.

David Lawrence described recent research which showed that people with psychiatric diagnoses are far more likely to smoke, and also to have difficulty in quitting. In Australia, people with mental illness smoke over 40% of all cigarettes consumed annually, and pay well over $2 billion in tobacco excise. Although higher rates of smoking also cost the health system billions each year, there is no evidence of any specifically targeted government intervention to help this section of the population to quit smoking.

Francis Mitrou spoke on smoking prevalence, mental disorders and emotional and behavioural problems in young people. The National Survey of Mental Health and Wellbeing found a strong correlation between emotional and behavioural problems among young people and their uptake of smoking, and the Raine Study (WA Pregnancy Cohort Study) found similar patterns.

What are the implications for public health? Around one-third of smokers have common mental illnesses such as depression, and these disorders are associated with earlier and higher uptake of smoking, heavier smoking and smoking for longer than the rest of the population, as well as lower quitting rates. While anxiety disorders may be a risk factor for beginning smoking, smoking itself may also be a risk factor for the development of some mental illnesses.

On Friday 24 September, Professor David Castle (St Vincent’s Hospital/University of Melbourne) gave a UWA Psychiatry Research Seminar on ‘Depression in schizophrenia: recognition and treatment’.

It is very common for clinicians in all areas across mental health to see symptoms of depression, social phobia or OCD simply as part of a person’s overall diagnosis of schizophrenia. Instead, a hierarchical approach to diagnosis, beginning with organic symptoms, allows the clinician to assess symptoms of other concurrent mental disorders which are more responsive to treatment, and whose amelioration can improve the person’s quality of life.

Part of the problem for the clinician is distinguishing between the negative symptoms of schizophrenia and the symptoms of clinical depression. There are many factors operating in schizophrenia which may mediate depression: social and psychological stressors, loss of income, alcohol and illicit drug use, and even the dysphoric effects or side-effects of some antipsychotic medications. Depression can occur in the schizophrenia prodrome, or may occur as part of the post-psychotic period.

There are a range of factors to consider in the differential diagnosis of depression in schizophrenia, including organic factors related to the illness, diet, prescription drug side effects, physical illnesses and sleep disorders. There are also risks associated with the concurrent use of some antidepressants and antipsychotics.

On Monday 18 October, Professor Stan Catts (University of Queensland) gave a CCRN Research Seminar presentation on ‘Psychosis Australia: making research work for consumers and their families’.

Mental health consumers are still the ‘poor relations’ of health care, with high mortality rates from preventable or treatable conditions such as cardiovascular diseases and cancers. Government spending on mental health Australia-wide has increased by 85% in real terms since 1993, and yet the premature mortality rate among mental health consumers continues to rise steadily.

Part of the problem is that mental illnesses do not follow clinically-understood patterns in the way that most physical diseases do. Whereas with cancer, the incidence and mortality rates are carefully monitored, there is no equivalent monitoring of the incidence and mortality rates among people with schizophrenia – even though people with schizophrenia generally die more than 20 years younger than the general population.

The answer may lie in more translational research – taking research findings and turning them into real solutions that can be used in the clinical setting. Professor Catts is advocating the formation of a peak research body called ‘Psychosis Australia’ to coordinate and promote national mental health research projects with clinically effective outcomes.
Neurosciences and operated jointly by the School and the North Metropolitan Area Mental Health Service.

Pathways of risk from conception to disease: the Western Australian schizophrenia high-risk e-Cohort

The way in which a person develops schizophrenia is complex: both genetic inheritance and environmental risk factors are involved. So far, no single environmental risk factor has been identified as having a major effect, although researchers have reported significant associations with a number of factors, including season of birth, pregnancy and birth complications, urbanicity, migration, ethnicity, stress, and cannabis use.

In Western Australia, a local research team headed by Professor Vera Morgan has been constructing and analysing a longitudinal, multi-generational high-risk ‘e-Cohort’ of children of women with psychotic disorders, which will provide information on a child’s exposure to both familial and environmental risks at different stages in their development. This study includes an extensive range of potential risk factors and risk mediators which could influence an individual’s mental health outcomes. The cohort has been called an e-Cohort as the major part of the study data collection is based on the use of electronic administrative health records.

The idea of studying a high-risk cohort in Western Australia was originally conceived by CCRN Director Professor Assen Jablensky who began the work to create the cohort in the mid-1990s. The current e-Cohort is composed of all the children born in Western Australia between 1980 and 2001 to mothers with a diagnosis of psychosis who have had an inpatient or outpatient contact recorded on the statewide psychiatric case register between 1966 and 2001. They are compared to all children born in Western Australia between 1980 and 2001 whose mother has had no known psychiatric contacts.

The key measures collected for the e-Cohort are the children’s high-risk status (having a mother with psychosis), exposure to obstetric complications, a range of additional exposures along the developmental pathway, and the children’s neuropsychiatric outcomes including birth defects, intellectual disability and psychiatric illness, especially a psychotic disorder.

The e-Cohort study has already produced some important findings:

- mothers with schizophrenia, bipolar disorder and unipolar depression experience an increased overall incidence of obstetric complications
- complications are more likely in births occurring after the mother has developed a psychotic illness, suggesting that changes in the mother’s behaviour, such as poor nutrition and substance use, may affect the unborn child
- women with schizophrenia were more likely to have babies with low birth weight, minor physical abnormalities and cardiovascular birth defects - regardless of the timing of onset of maternal psychosis relative to the index birth
- rates of rare syndromes, intellectual disability, and pervasive developmental disorders in high-risk children are well above population rates

An important outcome to date has been the translation of these research findings into clinical practice through a Western Australian Department of Health grant to design and evaluate an antenatal care intervention programme for women with severe mental illness. As a result, in 2008, a specialist Childbirth and Mental Illness antenatal clinic, the first of its kind in Australia, was established at King Edward Memorial Hospital, with the intervention package (Healthy Babies for Mothers with Serious Mental Illness) implemented in community mental health services throughout the state.

A team of UWA researchers, including CCRN’s Adjunct Professor Jo Badcock (right), has been awarded a prestigious UWA-UQ Bilateral Research Collaboration Award (BRCA).

The project, entitled ‘Establishing a UWA-UQ network for collaboration in autism research’, has been awarded $19,735 as seeding money to develop a full CRC grant application.

The BRCA is a new research award designed to generate collaborative research projects between UWA and the University of Queensland, and in this inaugural year it received over 40 applications.

Grant assessors have described the standard of the applications as “extremely high”, and congratulated the team on their “notable achievement” against such a strong field.

The UWA team are: Professor Murray Maybery, Winthrop Professor David Badcock, Adjunct Professor Jo Badcock, Dr Andrew Whitehouse, Winthrop Professor Mike Anderson, Professor David Ravine and Dr John Wray. The team will attend a workshop hosted by UQ early in 2011 to consolidate the collaboration, discuss future project proposals and facilitate immediate data-sharing.

**New Staff and Students:** Sarah Hescam has joined CCRN as a research student for the next 6 months, working with Professor Mathew Martin-Iverson. Tammy Hall has joined the North Wing team as a Research Assistant, working on the Australian Schizophrenia Research Bank project.

**Conferences:** The following CCRN staff and students will be presenting at these upcoming conferences—


- Assen Jablensky, ‘Nosological entities in psychiatry: an historical illusion or a real moving target?’ *Brain and Self. Psychiatric Nosology: Definition, History and Validity*, Copenhagen, 14-17 November 2010

- Jo Badcock, Milan Dragovic, Coleman Garrett, ‘Getting a grip on odd speech in schizophrenia’, *Australasian Society for Psychiatric Research*, Sydney, 5-8 December 2010

- Saruchi Chhabra, Jo Badcock, David Leung, Murray Maybury, ‘Context binding and hallucination predisposition’, *Australasian Society for Psychiatric Research*, Sydney, 5-8 December 2010

- Anna Waterreus, Vera Morgan, Jo Badcock, ‘Informed consent: not just what participants need to know but how we tell them. An example from the Australian National Survey of High Impact Psychosis (SHIP)’, *Australasian Society for Psychiatric Research*, Sydney, 5-8 December 2010

**New Autism Research Collaboration—UWA-UQ**

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**News and Notes**

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