New target for developing effective anti-depressants

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For the first time in a human model, scientists have discovered how anti-depressants make new brain cells. This means that researchers can now develop better and more efficient drugs to combat depression.

Previous studies have shown that anti-depressants make new brain cells, however, until now it was not known how they did it. In a study to be published in the journal *Molecular Psychiatry*, researchers from the Institute of Psychiatry, King's College London, show that anti-depressants regulate the glucocorticoid receptor (GR) - a key protein involved in the stress response. Moreover, the study shows that all types of anti-depressant are dependent on the GR to create new cells.

Depression is expected to be the second leading burden of disease world wide by the year 2020. Recent studies have demonstrated that depressed patients show a reduction in a process called 'neurogenesis', that is, a reduction in the development of new brain cells. This reduced neurogenesis may contribute to the debilitating psychological symptoms of depression, such as low mood or impaired memory. With as much as half of all depressed patients failing to improve with currently available treatments, developing new effective anti-depressant treatment still remains a great challenge, which makes it crucial to identify new potential mechanisms to target.

The Laboratory of Stress, Psychiatry and Immunology (SPI-lab) at King's has been looking into the role of the GR in depression for a number of years. In this study, scientists used human hippocampal stem

cells, the source of new cells in the human brain, as a new model to investigate 'in a dish' the effects of anti-depressants on brain cells.

Christoph Anacker, PhD student at the Institute of Psychiatry at King's and lead author of the study said: 'For the first time in a clinically relevant model, we were able to show that anti-depressants produce more stem cells and also accelerate their development into adult brain cells. Additionally, we demonstrate for the first time that stress hormones, which are generally very high in depressed patients, show the opposite effect.

'We discovered that a specific protein in the cell, the glucocorticoid receptor, is essential for this to take place. The anti-depressants activate this protein which switches on particular genes that turn immature 'stem' cells into adult 'brain' cells.

'By increasing the number of new-born cells in the adult human brain, anti-depressants counteract the damaging effects of stress hormones and may overcome the brain abnormalities which may cause low mood and impaired memory in depression.'

Anacker concludes: 'Having identified the glucocorticoid receptor as a key player in making new brain cells, we will now be able to use this novel stem cell system to model psychiatric illnesses in the laboratory, test new compounds and develop much more effective, targeted anti-depressant drugs. However, first it is important that future studies investigate all possible effects that the increase of neurogenesis has on behaviour in humans.'

Provided by King's College London