

## **NOVEL THERAPEUTIC OPPORTUNITIES IN UNIPOLAR DEPRESSION**

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Unipolar depression (UD) is a serious psychiatric medical illness that affects million of people of every race and ethnic group at every stage of life, with a life time of prevalence of 16%. UD is a complex and heterogeneous centrally mediated disease which symptomatically includes: a persistent sad mood, loss of interest or pleasure, significant change in appetite or body weight, difficulty sleeping or oversleeping; physical slowing or agitation; loss of energy; feelings of worthlessness or inappropriate guilt; difficulty thinking or concentrating and recurrent thoughts of death or suicide. Past biological research in psychiatry established the current antidepressants by increasing the brain levels of serotonin and noradrenalin. More recently, a reduction in hippocampal volume in depressed patients has pointed toward the decrease of brain neurogenesis as alternative or concomitant causes for the development of UD. Moreover, the hyperactivity of the hypothalamus pituitary adrenal axis observed in patients has been proposed as responsible for some UD symptoms. The biology of these processes suggests that novel antidepressants potentially more efficacious and safer than the existing ones could be developed by exploring drugs modulating neurotrophic and transcription factors, tachykinin receptors and hypothalamic peptides such as those that modulate the CRF and NPY systems. Novel antidepressant drugs might also be derived by genetic studies in search of endophenotypes, rather than just identifying diagnostic biomarkers per se. Endophenotypes provide means for identifying the downstream traits of clinical phenotypes, as well as the upstream consequence of genes. The methods available to identify endophenotypes include neuropsychological, cognitive, neurophysiological, neuroanatomical, endocrinological and biochemical measures. Using these evolving hypotheses of depression with the concept of genetically derived endophenotypes, improvements upon current medications may be envisaged for the future care of the patients who suffer from this debilitating disease.