

## INTERMEDIATE REPORT PUBLISHABLE EXECUTIVE SUMMARY

During the first reporting period of the PHECOMP project (February 2007-July 2008) **four animal models** of compulsive drug and/or food intake, namely, the **modified conflict** model for cocaine and morphine (in rats and mice), the alcohol **deprivation** model (in rats and mice), the **reinstatement** model for nicotine, cocaine and food (in mice) and the **compulsive food seeking/taking** model (in rats and mice), have been successfully well-characterised **phenotypically** employing pertinent **behavioural** paradigms. These models are addressing different components of compulsion, thus allowing further studies on compulsive behaviour to be performed by the scientific community and the pharmaceutical industry in search of new targets for treating these disorders. Parallel **molecular** analyses of brain samples coming from these four models have produced several preliminary results. For the reinstatement model, **Arc** and **Zif268** genes were markedly induced in different brain areas immediately after the reinstatement session in mice primed with cocaine. On the other hand, significant differences in comparison to the sham-treated control were found for **PDYN** in mice from the extinction group. In addition, the development and set up of the conditions for the manufacturing (synthesis, purification, formulation and quality control) of the radiotracers [<sup>11</sup>C]-Carfentanil, [<sup>11</sup>C]-JHU7528 and [<sup>11</sup>C]-GR103545 have been accomplished, the **validation of the pharmacological profile of [<sup>11</sup>C]-JHU7528** using wild type and CB1 knockout mice has been done and a **method for analysing mouse brain PET images applying partial volume correction** has been delivered. Furthermore, a **non-invasive imaging technique employing computed tomography** suitable to measure and visualize the **body fat content of small laboratory animals in vivo** has been reported. Moreover, the phenotypical characterisation of different strains of genetically modified mice targeting the glucocorticoid receptor (GR) gene in the dopaminergic transmission, e.g. GR<sup>NesCre</sup>, GR<sup>D1Cre</sup>, GR<sup>DATCre</sup> and *Eno2-ΔGR/EGFP*, has been completed for the **modified conflict** model for cocaine and for the **alcohol deprivation** model. Finally, a new food and drink monitoring system for mice has been designed, produced and successfully validated for the **reinstatement** and the **compulsive food seeking/taking** models.