

本セミナーは、HBS研究部・神経病態解析学分野 (准教授・笠原二郎)が不定期に主催するセミナー シリーズで、聴衆(特に若者)への刺激とブレイン ストーミングを目的に、ジャンルを問わず各界の 最前線でユニークな活躍をされている方々をお招 きし、お話し頂きます。研究部の多くの学部生・ 大学院生・教職員の参加をお待ちしております。

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シリーズ第14回 演者: Prof. Giorgio A. Racagni

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<u>演題</u>: Neuroplasticity and its influence on psychopathology in depression: role of antidepressant drugs

開催日時:2013 年 9 月 10 日(火) 17:00 - 18:30

開催場所:薬学部 2F 第 1 講義室 (スタジオプラザ 2 F)

脳科学クラスターセミナーを兼ねます。薬学部能動学習単位1ポイント付与。

イタリア神経精神薬理界の大物が来日されます。Giorgio Racagni 教授は、ミラノ大学の神経薬理学センター長や Dipartimento di Scienze Farmacologiche e Biomolecolari のディレクターなど様々な要職にあり、各種関連学会や学術誌の幹部も務めておられます。藤井大塚国際教育研究交流資金にて、本学薬学部と学部間交流協定締結などを目的に来日されますので、研究セミナーをお願いいたしました。皆様ふるってご参加下さい。

講演要旨

During the last decade, the idea of major depression as a condition characterized by impaired neuronal plasticity has been developed, suggesting that psychopathology may be associated with reduced expression and function of proteins that are important for cellular resilience, leading to enhanced vulnerability under "challenging situations" (Pittenger and Duman, 2008). Hence, it is feasible to hypothesize that conditions, such as those determined by a genetic impairment of serotonin transporter (SERT), that are associated with increased risk for depression, can lead to an impairment of the mechanisms that are important for neuronal plasticity and that may contribute to disease vulnerability. On this basis, we investigated if genetic abnormalities of the SERT can lead to alterations in the expression of brain-derived neurotrophic factor (BDNF), a neurotrophin that, because of the activity-dependent regulation of its expression and secretion (Bramham and Messaoudi, 2005), has emerged as crucial mediator of neuronal plasticity. BDNF is involved in the etiopathology of mood disorders as well as in the mechanism of action of antidepressant drugs (Berton and Nestler, 2006; Calabrese et al., 2007; Groves, 2007; Martinowich et al., 2007; Molteni et al., 2009), and a close link between serotonin and the neurotrophin has been suggested. In my presentation, we investigated the expression of BDNF in different brain regions from SERT mutant rats (+/- and -/-). Moreover, given the complex genomic structure of the neurotrophin (Aid et al., 2007), we have investigated the influence of SERT deletion on its different transcripts and evaluated the involvement of epigenetic mechanisms in their modulation. Finally, we have examined if alterations on BDNF expression were also present in human leukocytes from healthy individuals with different 5-HTTLPR genotypes.

References:

Aid, T., et al., 2007. Mouse and rat BDNF gene structure and expression revisited. J. Neurosci. Res. 85, 525–535.

Berton, O., Nestler, E.J., 2006. New approaches to antidepressant drug discovery: beyond monoamines. *Nat. Rev. Neurosci.* 7, 137–151. Bramham, C.R., Messaoudi, E., 2005. BDNF function in adult synaptic plasticity: the synaptic consolidation hypothesis. *Prog. Neurobiol.* 76, 99–125. Calabrese F, Molteni R, Maj PF, Cattaneo A, Gennarelli M, Racagni G, Riva MA., 2007. Chronic duloxetine treatment induces specific changes in the expression of BDNF transcripts and in the subcellular localization of the neurotrophin protein. *Neuropsychopharmacology* 32, 2351–2359. Groves, J.O., 2007. Is it time to reassess the BDNF hypothesis of depression? *Mol. Psychiatry* 12, 1079–1088.

Martinowich, K., et al., 2007. New insights into BDNF function in depression and anxiety. Nat. Neurosci. 10, 1089–1093.

Molteni R., Calabrese F., Cattaneo A., Mancini M., Gennarelli M., Racagni G. and Riva MA, 2009. Acute stress responsiveness of the neurotrophin BDNF in the rat hippocampus is modulated by chronic treatment with the antidepressant duloxetine. *Neuropsychopharmacology* 34, 1523–1532. Pittenger, C., Duman, R.S., 2008. Stress, depression, and neuroplasticity: a convergence of mechanisms. *Neuropsychopharmacology* 33, 88–109.