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Naples, Italy*

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# *European Journal of Histochemistry*

## *a journal of functional cytology*

The *European Journal of Histochemistry* was founded in 1954 by Maffo Vialli and published till 1979 under the title of *Rivista di Istochimica Normale e Patologica*, from 1980 to 1990 as *Basic and Applied Histochemistry* and in 1991 as *European Journal of Basic and Applied Histochemistry*. It is now published under the auspices of the University of Pavia, Italy.

The *European Journal of Histochemistry* is the official organ of the Italian Society of Histochemistry and a member of the journal subcommittee of the International Federation of Societies for Histochemistry and Cytochemistry (IFSHC), and has been an influential cytology journal for over 60 years, publishing research articles on functional cytology and histology in animals and plants.

The Journal publishes Original Papers, Technical Reports, Reviews, Brief Reports, Letters to the Editor, Views and Comments, and Book Reviews concerning investigations by histochemical and immunohistochemical methods, and performed with the aid of light, super-resolution and electron microscopy, cytometry and imaging techniques; attention is also given to articles on newly developed or originally applied histochemical and microscopical techniques.

Coverage extends to:

- functional cell and tissue biology in animals and plants;
- cell differentiation and death;
- cell-cell interaction and molecular trafficking;
- biology of cell development and senescence;
- nerve and muscle cell biology;
- cellular basis of diseases.

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## IMPACT OF EARLY-LIFE STRESS AND GONADAL HORMONES ON REWARD SYSTEMS OF ABA RATS

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Anorexia nervosa (AN) is a psychiatric illness in which the main symptoms are a disrupted perception of the body and its shape and disturbed eating that leads to self-starvation. A disturbance of the brain serotonergic network predates the onset of AN and should contribute to premorbid symptoms of anxiety, inhibition, and vulnerability to dietary restrictions. Moreover, puberty-related steroids and stress may enhance serotonin (5-HT) and dopamine (DA) dysregulation and aggravate the disease. In fact, these two systems are of greater interest in AN because their central pathophysiological role in patients is still limited. Based on our previous study, here we investigate the effects of early-life stress and of the absence of gonadal hormones in Activity Based Anorexia (ABA) affected rats. Four groups of gonadectomized (GDX) rats (GDX, MS-GDX, ABAGDX, MS-ABA-GDX) of both sexes were used, applying maternal separation (MS) to mild stress induction (3 hours/day, from PND1 to PND15) and the ABA protocols (2 hours of running wheel followed by 1 hour of food access, from PND37 to PND42) to provide symptoms like hyperactivity and weight loss, resembling anorectic patients' conditions. The exploratory and anxiety-like behaviours were evaluated using the open field (OF) and elevated plus maze (EPM) tests. Last, to investigate the impact on serotonergic and dopaminergic systems, immunohistochemical analysis was performed to quantify the presence of 5-HT in the dorsal raphe nucleus (DRN) and median raphe nucleus (MRN) and of the DA in the ventral tegmental area (VTA) and substantia nigra (SN). The ABA protocol induced hyperactivity and a reduction in anxiety-like behaviours in rats of both sexes compared to controls (GDX). In addition, the behavioural phenotype alteration appeared to be sex-dependent by combining MS and ABA in GDX rats. Of particular interest were the results of 5-HT+ cells in GDX rats that changed from MS and ABA, or the combination of the two, showing distinct effects in the two sexes, especially in the dorsal part of DRN. Although serotonergic and dopaminergic systems in anorexic rats develop in the presence of gonadal hormones, their suppression may have altered the activation of those systems, whereas MS may have affected their organization, influencing the behaviour observed in ABA rats.

## S100B PROTEIN AND MICROBIOTA

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S100B is a small EF-hand calcium-binding protein expressed by definite neural and extraneural cell types, being also present in enteroglial cells and in the enteric nervous system-ENS. Notably, it has been detected in biological fluids as a biomarker. It belongs to the S100 family that is located as a cluster on chromosome 1q21, while *S100B* gene is located at 21q22.3 and codifies for a multifunctional protein involved in several physiological processes. Modulations of *S100B* have been implicated in several disorders and pathogenetic pathways, including inflammatory processes and extracellular activity interacting with the Receptor for Advanced Glycation Endproducts. S100B was detected in the intestinal lumen and in feces of healthy individuals (Di Liddo et al 2020), but also associated to amplification of the *Clostridium difficile* toxin-induced colonic damage in Inflammatory Bowel Disease (IBD). In previous *in silico* studies, we showed the differential capability of S100B to interact with the proteome of a healthy microbiota (Orsini et al 2020), suggesting a possible role at the mucosa-microbiota barrier, in the ENS and in the gut microbiota axis. Our *in vivo* experiments in mouse models disclosed a relationship between S100B levels and microbiota biodiversity, further supporting the hypothesis of a possible interaction with the mechanisms involved in gut microflora equilibrium. Consistently, S100B-dependent effects on microbiota could not be observed in presence of drugs interfering with S100B functional pathways, such as Pentamidine. The relative occurrence of bacteria at risk for IBD such as *Clostridium* was also influenced by the presence of the protein, suggesting a putative protective role of S100B in the gut lumen. The whole of the observed results supports a role for S100B in the microflora equilibrium and opens new perspectives proposing S100B as a therapeutic target for the modulation of gut microbiota axes and disease pathways, including IBD and several chronic conditions.