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“Gruppo Italiano per lo Studio  
della Neuromorfologia” G.I.S.N.**

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Naples, Italy*

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under the auspices of  
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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;
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- nerve and muscle cell biology;
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**November 25-26, 2022**

***University of Campania, Luigi Vanvitelli  
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## BISPHENOLS AS NEW ENVIRONMENTAL RISK FACTORS IN MULTIPLE SCLEROSIS

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Epidemiological studies support the idea that multiple sclerosis (MS) is a multifactorial disease overlapping genetic, epigenetic, and environmental factors. A better definition of environmental risks is critical to understand both the aetiology and the sex-related differences of MS. Exposure to Endocrine Disrupting Compounds (EDCs) fully represents one of these risks. EDCs are natural or synthetic exogenous substances (or mixtures) that alter the functions of the endocrine system. Among synthetic EDCs, exposure to bisphenol A (BPA) has been implicated in the aetiology of MS, but controversial data has emerged to date. Furthermore, nothing is known about bisphenol S (BPS), one of the most widely used substitutes for BPA. As exposure to bisphenols will not disappear soon, it is necessary to clarify their role in this pathological condition, defining their impact on disease onset and progression. In this study, we examined, in both sexes, the effects of perinatal exposure to BPA and BPS in one of the most widely used mouse models of MS, experimental autoimmune encephalomyelitis (EAE). Exposure to bisphenols seemed to be particularly deleterious in males. In fact, both BPA- and BPS-treated males showed anticipation of the disease onset and an increased motoneuron loss in the spinal cord. Overall, BPA-treated males also displayed an exacerbation of the EAE course and an increase in inflammation markers in the spinal cord. Among females, the treatments did not significantly affect the analysed disease-related parameters, confirming the sex-specific effects of perinatal exposure to bisphenols also in this pathological condition. Analysing the consequences of bisphenols exposure on EAE will help better understand the role of both xenoestrogens and endogenous estrogens on the sexually dimorphic features of MS.

## BENEFICIAL EFFECTS OF MSC TREATMENT ON CCL2-MICROGLIA-MEDIATED CEREBRAL CORTEX NEUROINFLAMMATION: EMERGING ROLES FOR MSC-DERIVED EXTRACELLULAR VESICLES

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Experimental autoimmune encephalomyelitis (EAE) in mouse

neocortex is characterized by inflammation, demyelination and blood-brain barrier (BBB) dysfunction. Treatment with mesenchymal stem cells (MSCs) ameliorates the clinical course of EAE, significantly reducing neuroinflammation, demyelination and astrogliosis, while improving BBB function. In the present study, using the same experimental model of EAE-affected MSC-treated mice, we have investigated the cellular sources of CCL2, a chemokine claimed to be primarily expressed by astrocytes and endothelial cells, involved in leukocytes recruitment and BBB impairment during neuroinflammation. The analysis was carried out by immunohistochemistry (IHC) and dual RNAscope IHC/*in situ* hybridization, using novel microglia-specific markers, *i.e.* TMEM119 and SALL1, combined with astrocytic- and endothelial-specific markers and with antibody against CCL2. The results show the presence of activated hypertrophic microglia cells, which express high levels of CCL2 in the EAE mouse neocortex. Microglia activation and CCL2 expression in MSC-treated and untreated EAE mice, have been evaluated and compared by morphometric parameters. According to these results, the neocortex of EAE-affected MSC-treated mice is characterized by a reduced microglia reactivity and a lower CCL2 expression, together with restored BBB structure and function. The role of MSCs and the possible mechanism by which these cells counteract neuroinflammation was further investigated, transfecting these cells with GFP lentivirus and analyzing their viability at the level of the mouse lungs, a site where MSCs are known to be trapped. The results show that, after venous administration, MSCs localize, in both control and EAE mice, within the alveolar septa. MSCs detected in EAE-affected mouse lungs express the multivesicular body marker CD9 and seem to release extracellular vesicles (EVs). The idea that MSC-derived EVs may be involved in the effectiveness of MSC treatment, through the interaction with endothelial cells, was supported by the immunodetection of the MSC marker endoglin (CD105). The observed clustering of endoglin at the endothelium-MSC interface indicates the glycoprotein as a potential partner in endothelium-MSC interaction and suggests a possible mechanism of MSC-derived EV release at the alveolar interstitium-capillary barrier.

## THE S100B PROTEIN AS A THERAPEUTIC TARGET FOR MULTIPLE SCLEROSIS PROCESSES

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S100B is a calcium-binding protein mainly concentrated in astrocytes. Its levels in biological fluids are recognized as a reliable, even predictive, biomarker of active neural distress. Mounting evidence now points to S100B as a Damage-Associated Molecular Pattern protein which, when released at high concentration, triggers tissue reaction to damage in various disorders.<sup>1,2</sup>

A number of correlative evidence proposes that S100B high lev-