

DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

42° CYCLE

Project proposal for a Sapienza PhD scholarship

Main research line

Title: Interplay between Oxytocin Signaling and Neuroinflammation in Social Context Modulation in a Mouse Model of 22q11.2 Deletion Syndrome

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Summary

Autism spectrum disorder (ASD) is characterized by altered social behavior, stress responsivity, and neuroimmune imbalance. Increasing evidence suggests that the social environment critically influences behavioral and physiological outcomes, potentially through modulation of stress-regulatory and immune pathways.

Oxytocin (OXT), a key neuromodulator of social and emotional processing, has been implicated in these processes; however, the interaction between social context, oxytocin signaling, and neuroinflammatory mechanisms in ASD remains poorly defined.

22q11.2 deletion syndrome (22q11.2DS) represents one of the strongest genetic risk factors for ASD. The LgDel/+ mouse model reproduces behavioral, synaptic, and immune alterations relevant to the human condition.

This project aims to investigate how modulation of the social environment and oxytocin signaling influence socio-cognitive performance and stress responses in this model, and to determine whether these effects involve changes in central and peripheral immune regulation as well as synaptic plasticity mechanisms.

By integrating behavioral, molecular, and electrophysiological approaches, the study will explore how environmental and neurobiological factors interact in shaping ASD-related phenotypes. The findings are expected to contribute to a better mechanistic understanding of context-dependent modulation of neurodevelopmental disorders and to support the development of translational strategies.

Pertinent Publications of the proponent (last 5 years)

1. Castellani G*, Ciampoli MS*, Benedetti A *, **Ferretti V***, Trigilio G, Barcik W, Busnelli M, Contarini G, Paolino C, Devroye C, Maltese F, Braccia C, Pacinelli G, Manago' F, Sannino S, Albanesi E, Nigro M, Armirotti A, De Martin S, Chini B, Papaleo F. Oxytocin Seals the Brain Barriers Ameliorating the Immune-Behavioral Trajectories in 22q11.2 Deletion Syndrome. *Brain* doi: 10.1093/brain/awaf112.
2. Ferrucci L, Basilico B, Reverte I, Pagani F, Scaringi G, Cordella F, Cortese B, De Propis G, Galeone A, Mazzarella L, Mormino A, Garofalo S, Khan A, De Turris V, **Ferretti V**, Bezzi P, Gross C, Caprioli D, Limatola C, Di Angelantnio S, Ragozzino D. Time-dependent Phenotypical Changes of Microglia Drive Alterations in Hippocampal Synaptic

Transmission in Acute Slices. *Frontiers in Cellular Neuroscience* doi: 10.3389/fncel.2024.1456974

3. Mastrogiacomo R, Trigilio G, Devroye C, Dautan D, **Ferretti V**, Losi G, Caffino L, Orso G, Marotta R, Maltese F, Vitali E, Piras G, Forgiarini A, Pacinelli G, Lia, A, Rothmond D, Waddington J, Drago F, Fumagalli F, Papaleo F. (2022). Dysbindin-1A modulation of astrocytic dopamine and basal ganglia dependent behaviors relevant to schizophrenia. *Molecular Psychiatry* 1-17.doi: 10.1038/s41380-022-01683-8.
4. Lufy, K., Hipolito, L., **Ferretti, V.**, Vendruscolo, L.F., Kallupi, M.(2022). Editorial: The Role of Neuropeptides in Drug Addiction and Other Psychiatric Disorder. *Frontiers in Behavioral Neuroscience*, 16, 952551
5. De Stefano ME, **Ferretti V**, Mozzetta C (2022) Synaptic alterations as a neurodevelopmental trait of Duchenne muscular dystrophy. *Neurobiology of Disease* 168, 105718
6. Basilico B, Ferrucci L, Ratano P, Golia MT, Grimaldi A, Rosito M, **Ferretti V**, Reverte I, Sanchini C, Marrone, MC, Giubettini M, De Turrís V, Salerno D, Garofalo S, St-Pierre MK, Carrier M, Renzi M, Pagani F, Modi B, Raspa M, Scavizzi F, Gross C T, Marinelli S, Tremblay ME, Caprioli D, Maggi L, Limatola C, Di Angelantonio S, Ragozzino D. (2021) Microglia control glutamatergic synapses in the adult mouse hippocampus *GLIA* 70(1):173-195 doi: <https://doi.org/10.1002/glia.24101>
7. Scheggia D*, Managò F*, Maltese F, Bruni S, Nigro M, Dautan D, Latuske P, Contarini G, Gomez-Gonzalo M, Reque LM, **Ferretti V**, Castellani G, Mauro D, Bonavia A, Carmignoto G, Yizhar O & Papaleo F (2020). Somatostatin interneurons in the prefrontal cortex control affective state discrimination in mice. *Nature Neuroscience* 23, 47–60, doi:10.1038/s41593-019-0551-8