

DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

42° Cycle

Project proposal for a PhD scholarship

Main research line

Title of the research: Modeling the complex interaction of emerging viruses with the genital tract in 2D and 3D-human based cell culture systems

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Summary (max 500 words)

In recent years, it has become clear that sexual and/or vertical transmission can represent alternative routes of spread for a wide range of emerging or re-emerging viruses such as Zika, Ebola, Monkeypox, and Oropouche virus. The factors that determine the potential for sexual transmission include their presence and persistence in genital fluids, the susceptibility of mucosal surfaces that represent entry sites for the virus (e.g., cervico-vaginal tract, urethra, rectum), and viral replication within the genital tract. Replication in the female genital tract (FGT), in addition to impact sexual and reproductive health, can also lead to vertical transmission.

The mechanisms of infection of the FGT have been extensively studied for major sexually transmitted viruses (HIV, HPV, HSV) less in depth for Zika virus, whereas they remain largely unexplored for other emerging pathogens including other flaviviruses, bunyaviruses (e.g. Oropouche), or monkeypox virus whose presence in genital fluids, sexual and/or vertical transmission have been described.

In this project, we aim to implement physiologically relevant three-dimensional (3D) cellular models of the lower and upper FGT to dissect the mechanisms of infection. The interaction with host cellular and humoral factors capable of modulating and/or being modulated by infection—such as the immune and stromal cells, sex hormones, and the microbiome—will be analyzed in the developed models applying targeted and omics approaches.

The emerging viruses selected as models for these analyses include primarily Zika, and Oropouche virus. By leveraging 3D culture systems, we aim to generate insights of greater translational relevance than those achievable with traditional monolayer models, ultimately contributing to a deeper understanding of mucosal infection mechanisms and informing strategies for prevention and therapeutic intervention.

Pertinent Publications of the proponent (last 5 years):

1. Picarone L, Pietrucci D, Mariotti D, Milanese M, Mija C, Bordi L, Meschi S, Mazzotta V, Gruber CEM, Mavian C, Girardi E, Antinori A, **Matusali G***, Chillemi G*, Maggi F Mapping transcriptional patterns of MPXV in human epithelial cells. *Emerg Microbes Infect.* 2026 Dec;15(1):2627079. doi: 10.1080/22221751.2026.2627079. *corresponding author
2. Vita S, Colavita F, Maffongelli G, Carletti F, Scorzoloni L, **Matusali G**, Tomassi MV, Meschi S, D'Abramo A, Girardi E, Vairo F, Maggi F, Nicastrì E; INMI Arbovirosi Group Viral shedding in saliva, axillary, rectal and vaginal swabs of an imported case of Dengue - Oropouche virus Co-infection. *Travel Med Infect Dis.* 2025 Jul-Aug;66:102854. doi: 10.1016/j.tmaid.2025.102854.

3. **Matusali G**, Manica M, D'Abramo A, Carletti F, Maffongelli G, Colavita F, Poletti P, Lalle E, Sberna G, Specchiarello E, Bordi L, Meschi S, De Carli G, Spaziante M, Corpolongo A, Girardi E, Merler S, Vairo F, Nicastrì E, Maggi F; Study Group on Arboviruses. Dengue Virus Dynamic and Persistence in Body Fluids of Infected Patients in Italy, 2018-2023. *J Med Virol.* 2025 Apr;97(4):e70322. doi: 10.1002/jmv.70322.
4. Meschi S, Colavita F, Carletti F, Mazzotta V, **Matusali G***, Specchiarello E, Ascoli Bartoli T, Mondì A, Minosse C, Giancola ML, Pinnetti C, Valli MB, Lapa D, Mizzoni K, Sullivan DJ, Ou J, Focosi D, Girardi E, Nicastrì E, Antinori A, Maggi F. MPXV DNA kinetics in bloodstream and other body fluids samples. *Sci Rep.* 2024 Jun 12;14(1):13487. doi: 10.1038/s41598-024-63044-5 *corresponding author
5. Lapa D, Carletti F, Mazzotta V, **Matusali G**, Pinnetti C, Meschi S, Gagliardini R, Colavita F, Mondì A, Minosse C, Scorzolìni L, Cicalini S, Maffongelli G, Specchiarello E, Camici M, Bettini A, Baldini F, Francalancia M, Mizzoni K, Garbuglia AR, Nicastrì E, Girardi E, Antinori A, Vaia F, Maggi F; INMI Monkeypox Study Group. Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding. *Lancet Infect Dis.* 2022 Sep;22(9):1267-1269. doi: 10.1016/S1473-3099(22)00513-8.
6. **Matusali G**, D'Abramo A, Terrosi C, Carletti F, Colavita F, Vairo F, Savellini GG, Gandolfo C, Anichini G, Lalle E, Bordi L, Corpolongo A, Maritti M, Marchioni L, Capobianchi MR, Castilletti C, Cusi MG, Nicastrì E. Infectious Toscana Virus in Seminal Fluid of Young Man Returning from Elba Island, Italy. *Emerg Infect Dis.* 2022 Apr;28(4):865-869. doi: 10.3201/eid2804.211920
7. Bordoni V, **Matusali G**, Mariotti D, Antonioli M, Cimini E, Sacchi A, Tartaglia E, Casetti R, Grassi G, Notari S, Castilletti C, Fimia GM, Capobianchi MR, Ippolito G, Agrati C. The interplay between SARS-CoV-2 infected airway epithelium and immune cells modulates regulatory/inflammatory signals. *iScience.* 2022 Feb 18;25(2):103854. doi: 10.1016/j.isci.2022.103854.
8. **Matusali G**, Trionfetti F, Bordoni V, Nardacci R, Falasca L, Colombo D, Terri M, Montaldo C, Castilletti C, Mariotti D, Del Nonno F, Capobianchi MR, Agrati C, Tripodi M, Strippoli R. Pleural Mesothelial Cells Modulate the Inflammatory/Profibrotic Response During SARS-CoV-2 Infection. *Front Mol Biosci.* 2021 Nov 26;8:752616. doi: 10.3389/fmolb.2021.752616.