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## Binding of fusion protein FLSC IgG1 to CCR5 is enhanced by CCR5 antagonist maraviroc

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The CCR5 chemokine receptor is crucial for human immunodeficiency virus type 1 (HIV-1) infection, acting as the principal coreceptor for HIV-1 entry and transmission and is thus an attractive target for antiviral therapy. Studies have suggested that CCR5 surface density and its conformational changes subsequent to virion engagement are rate limiting for entry, and consequently, infection. Not all CCR5 antibodies reduce HIV-1 binding, entry and infection, suggesting a need for more potent reagents. Here full length single chain (FLSC) IgG1, a novel CD4-gp120BAL fusion protein with several characteristics was evaluated that makes it an attractive candidate for treatment of HIV-1 infections, including bivalency and a potentially increased serum half-life over FLSC itself. FLSC IgG1 binds two domains on CCR5, the N-terminus and the second extracellular loop, lowering the levels of available CCR5 viral attachment sites. Furthermore, FLSC IgG1 is synergistic with Maraviroc, the only one licensed CCR5 antagonist. In this study, both, microscopy and functional assays were used to address the mechanistic aspects of the interactions of FLSC IgG1 and Maraviroc in the context of CCR5 conformational changes and viral infection. A novel Stochastic Optical Reconstruction Microscopy (STORM) was used based on high-accuracy of photoswitchable dyes localization with high resolution to visualize direct contacts between FLSC IgG1 and CCR. Viral entry inhibition by FLSC IgG1 with that of other CCR5 blockers was compared and showed FLSC IgG1 to be the most potent. Also it was also shown that lower CCR5 surface densities in HIV-1 infected primary cells result in reduced FLSC IgG1 EC50 values. In addition, CCR5 binding by the FLSC IgG1, but not by 2D7, was significantly increased when cells were treated with MVC, suggesting MVC increases exposure of the relevant epitope. Together, this data may have implications on future anti-viral therapy efforts.

### Biography

Olga Latinovic received her M. Sc (2001) and PhD (2006) from Lehigh University, USA, where she was awarded the Sherman Fairchild scholarship for outstanding academic performance. As of 2010, she is an assistant professor working at the Institute of Human Virology led by Robert C. Gallo, MD at the University of Maryland, School of Medicine in Baltimore, USA. She heads the Laboratory for Imaging Studies of Pathogens and Host Cells Interactions. Dr. Latinovic's research focus is on HIV-1 entry and its inhibition into host target cells, particularly focusing on the CCR5 coreceptor which plays a major role in HIV-1 infection and is consequently an attractive target for anti-viral therapy. Dr. Latinovic wrote the book Micromechanics and Structure of Soft and Biological Materials, as a sole author and published by Verlag Dr. Muller in 2010, and co-authored the book Handbook of Photonics for Biomedical Engineering published bySpringer-Verlag in 2013. Dr. Latinovic lectures Virus Entry course for the grad students at the Department of Microbiology and Immunology at the University of Maryland and she has lectured at various national/international conferences, and is on the Editorial Board of three scientific journals. She is a member of several national and international scientific societies.

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## Acute radiation-combined syndrome: Immunological profile and response to therapeutic interventions

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Victims of nuclear disasters often suffer from a radiation injury (RI) combined with other types of injury; radiation-combined injury (CI). Medical countermeasures proposed for RI are not necessarily effective for CI, and vice versa. There is a strong need to identify pathology specific to CI and plan for effective treatments. The talk will summarize current CI research with respect to: An animal model, a unique pathology including immunological aspects, and medical countermeasures that have been tested. These together may direct us to prospective CI management.

### Biography

Risaku Fukumoto has completed his PhD at the age of 28 years from the University of Tokyo and Postdoctoral studies from the National Institutes of Health. He is the lead scientist of Armed Forces Radiobiology Research Institute in the University. He has published more than 10 papers in a few years of current affiliation and is serving as an international editor of the *Journal Progress in Health Sciences*.

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