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# Abstracts of ECI 2021

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## POSTER PRESENTATIONS

## P-0887

## Extracellular vesicles subtypes in sera of COVID-19 patients as indicators of immune dysregulation and disease severity

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COVID-19 is characterized by a wide spectrum of disease severity, ranging from asymptomatic to critical symptoms, hallmarked by immune dysregulation. Despite intensive investigations, the underlying mechanisms, and indicators of COVID-19 immunopathogenesis are largely missing. Extracellular vesicles (EVs) emerged as key mechanisms of cell-to-cell communication and excellent biomarkers in many infectious and immune-related diseases. However, their role COVID-19 is largely unknown. Here we analyzed a set of clinical, biochemical and immunological markers in 46 COVID-19 patients (20 with mild symptoms, and 26 with severe symptoms) and 16 sex/age-matched healthy individuals, along with the imaging flow cytometry EVs characterization from donors' sera. We found an increased number of CD13+ EVs/ml in COVID-19 patients, and their number was significantly higher in the group of severe patients, along with the number of CD82+ EVs. Additionally, the number of CD13+ EVs positively correlated with the number of inflammatory monocytes and IL-6-producing myeloid-derived suppressor cells (MDSCs) in severe COVID-19 patients. In contrast, the patients with mild COVID-19 symptoms displayed an increased number of HLA-ABC+ EVs compared to healthy donors, and significantly higher number of CD24+ EVs, compared to severe COVID-19 patients. HLA-DR-ABC+ EVs and CD24+ EVs predicted positive outcome of COVID-19, as they negatively correlated with disease severity and accumulation of IL-10-producing MDSCs, the mediators of immune paralysis in severe COVID-19 patients. These results indicate for the first time that EVs in sera are excellent indicators of COVID-19 pathogenesis and disease progression, but the exact mechanisms underlining EVs actions in COVID-19 require further investigations.

**Keywords:** Biomarkers, chronic inflammation and fibrosis, endo- and exocytic vesicles in immunity

## P-0888

## Impaired LAIR-1-mediated immune control due to collagen degradation in systemic sclerosis

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Fibrosis is characterized by the production and deposition of excessive extracellular matrix (ECM) products such as collagen. Systemic sclerosis (SSc), is a potentially fatal disease characterized by immune dysregulation and fibrosis of the skin and internal organs. LAIR-1 is an inhibitory collagen receptor highly expressed on immune cells in these tissues. We show that LAIR-1 deficient mice have increased bleomycin-induced skin fibrosis, supporting a protective role for LAIR-1 in controlling fibrosis. In SSc patients, LAIR-1 expression and function is intrinsically normal. However, the ECM produced by fibroblasts of SSc patients contains high levels of collagen degradation products that can act as decoy ligand and impair LAIR-1 mediated signalling. These collagen degradation products are dependent of matrix metalloproteinases and platelet-derived growth factor (PDGF) receptor signalling. We conclude that LAIR-1 represents a control mechanism in tissue remodelling and that the absence of LAIR-1 mediated control in SSc patients results in a perpetuating loop in which fibrosis continues. The presence of functional LAIR-1 in SSc patients provides a therapeutic opportunity that holds promise for disease control.

**Keywords:** Checkpoint inhibition, chronic inflammation and fibrosis, tissue damage and repair

## P-0889

Multiple effects of *Alchemilla vulgaris* L. extract on melanoma cells and tumor microenvironmentSanja Jelača<sup>1</sup>, Dijana Drača<sup>1</sup>, Zora Dajić Stevanović<sup>2</sup>, Ivan Jovanović<sup>3</sup>, Sladjana Pavlović<sup>3</sup>, Nevena Gajović<sup>3</sup>, Sanja Mijatović<sup>1</sup>, Nebojša Arsenijević<sup>3</sup>, Danijela Maksimović Ivanić<sup>1</sup><sup>1</sup>Department of Immunology, Institute for Biological Research "Siniša Stanković" – National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia<sup>2</sup>Faculty of Agriculture, University of Belgrade, Belgrade, Serbia<sup>3</sup>Center for Molecular Medicine and Stem Cell Research, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

Several ethnobotanical reports on *Alchemilla vulgaris* L. pointed out diverse biological properties against problems such as dysmenorrhea, pruritus vulvae, menopausal complaints as well as related diseases in women. Also previous studies have shown that *Alchemilla vulgaris* L. extracts are exhibiting antiinflammatory, antioxidant, wound healing and neuroprotective activity. The aim of this study was to evaluate the direct effect of *Alchemilla vulgaris* L. ethanol extract against melanoma cells *in vitro* and *in vivo*, as well as its effect on tumor microenvironment *ex vivo*. This study was performed on two different mouse melanoma cell lines, B16 and B16F10, and on syngeneic mouse melanoma model *in vivo*. Obtained results revealed dose-dependent decrease of cell viability after 72 h- treatment with *Alchemilla vulgaris* L. extract. The observed effect was followed by loss of dividing potential in both tested cell lines. In parallel with this, certain percentage of B16F10 cells was subjected to programmed cell death in a caspase independent manner while in B16 cells estimation of the presence of autophagosomes by flow cytometry has shown that autophagy is occurring after the treatment and it is shown to be mechanism of death. Concerning *in vivo* studies *Alchemilla vulgaris* L. extract significantly reduced tumor growth in B16 melanoma model partly through stimulation of antitumor immune response. It altered dendritic cells phenotype which activated cytotoxic and CD4+ T lymphocytes to successfully destroy tumor cells. In summary, these data indicate that *Alchemilla vulgaris* L. is valuable of further investigation in the field of experimental oncology.

**Keywords:** Cancer immunology, cell death, *in vivo* tumor models, microenvironment