<table>
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<th>Project code</th>
<th>Host institution</th>
<th>PhD enrolment</th>
<th>Start date</th>
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<tr>
<td>ESR2</td>
<td>University of Padova (UNIPD)</td>
<td>Yes</td>
<td>January 1, 2022</td>
<td>36 months</td>
<td>Biomedical Sciences</td>
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**Project Title**: Protein composition and functional effects of the species-specific biomolecular corona formation on NPs  

**Supervisor**: E. Papini (UNIPD); co-supervisor: S.M. Moghimi (UNEW)  
SME co-supervisor: A. Falk (BNN) – WP2, WP3  

**Background and objectives**: NPs in the body fluids interact with host macromolecules and this strongly influences the NPs host-interaction and efficacy. Among proteins, Ca2+/Mg2+ dependent complement-derived ones are major protagonists leading to inflammatory mediators and to opsonine deposition. Closely related mammalian species used as preclinical models (e.g. mouse and pigs), evolved differentiated reactivity and organization of Complement and other innate mechanisms, which could negatively impact extrapolations to the human being. The goal of this ESR is extensively mapping the corona composition formed in human and animals sera, according to the coat type and evaluating Ca2+/Mg2+ dependence to monitor complement activation and abundance. We will probe the effect of putative pro-opsonic agonists (e.g. collections) with antagonists (e.g. N-acetyl-glucosamine or mannose) or compound mimicking monomers of the NP-covering polymers (e.g. N,N-dimethyl acetyl-amide in case of PMOXA coats) on NP proteoma and phagocytes capture. The effect of anti-corona protein mab (native or engineered) or recombinant engineered coat-binding innate proteins (e.g. the increase the number of conditions studied and the robustness of quantification and considerably reduces times. After initial protein abundance screening by label-free parameters major and functionally relevant components will be assessed by quantitative proteomics approaches or WB. In case of commercial antibodies lack, polyclonal/monoclonal ab will be generated by STABVIDA (ESR11). Recombinant antibodies-based assays will be also applied for validation, to immune-deplete sera and test biochemical and functional effects. Modulation of the binding of specific components to a coats will be also obtained via use of known innate-recognized sugars or by using single molecules resembling the NP polymer coats unit (for example dimethyl amide for PMOXA). Phagocytosis will be quantified by FACS and confocal analysis (Ope retta).  

**Risks**: (1- high): Absence of specific species-specific antibodies to NP corona proteins or complement components for mouse or pig, do validate proteomics - mitigation: clone the gene and purify the recombinant protein of interest (in collaboration with A: Negro ESR3 at UNIPD) and lend to STABVIDA for mab or polyclonal generation. Alternatively, in collaboration with F. Corzana (ESR14 UR) generate peptides derived from the primary sequence of the protein and obtain antibodies from STABVIDA, as above; (2- low) Influence of serum collection and generation in humans and animals - mitigation: define a standard protocol and check with specific assays the integrity of critical pathways like complement (in collaboration with SM Moghimi, ESR4, UNEW).  

**Expected results**: providing information on the major functional pro-opsonic and pro-inflammatory innate component affinity to coats type and suggest feedback modification of their formulation to test the possibility of its abolition (stealth) or improvement (nanovaccine). Reveal major species-specific molecular differences and point to NP characteristics showing interspecific similarity, for safer preclinical predictive power.  

**Planned secondment(s)**: 1) OUS, (G.M. Malandsom) to learn TAM targeting in murine models to allow training in methodologies used to assess in vivo distribution of NPs and on the evaluation of selective capture to defined TAM phenotype, month 12, 3 months. 2) PLUS (J. Horeis-Hoek) to be trained on the capture analysis of macrophage related but functionally different antigen presenting cells, like DCs, month 24, 3 months.  

**PhD award**: UNIPD  

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