SYNOPSIS OF THE CV Francesca Re

Francesca Re graduated in Medical Biotechnology from the University of Milano-Bicocca (UNIMIB) in 2005 and in 2008 completed a PhD degree in Neuroscience at UNIMIB with research conducted at the Laboratory of Biochemistry, School of Medicine and Surgery (Monza) under the supervision of Prof. Massimo Masserini (UNIMIB). From 2009, she worked with Prof. Massimo Masserini, a world-leading laboratory in Neuro-Nanomedicine, for a 6-year post-doctoral period. Starting 2015, she is creating her independent line of research at UNIMIB and currently she is associated professor of biochemistry and nanomedicine at UNIMIB. During her scientific career, F.R. has published 60 articles in top international peer-reviewed journals (including high IF journals). Her *h*-index is 23 and she has 1500 citations (Scopus). F.R. made important advances in the field of the search for ligands to target and overcome the blood-brain barrier (BBB) in order to design nanoparticles carrying drugs for CNS disorders, i.e. Alzheimer's disease, during her post-doctoral stay at the UNIMIB, as part of a research project funded by the European Community (NAD "Nanoparticles for therapy and diagnosis of Alzheimer's disease" from 2008 to 2013 FP7-NMP-2007-LARGE-1). This research resulted in 18 articles published in collaboration with different EU partners. Of note, F.R. had 3 career breaks between 2009 and 2016 due to maternity leave and was absent from research during approximately 15 months. Throughout her career, F.R. mainly focused in understanding the mechanisms to cross the BBB by macromolecules and nanoparticles and, most recently, to study new strategies to boost the amyloid-β peptide clearance from the brain across the BBB, as potential therapy for Alzheimer's disease. She has also acquired skills is the study of nanoparticles protein corona composition and its implication in the BBB crossing. F.R. has been able to attract funding from prestigious European entities, being a recipient of a H2020 Project funded by EU Joint Programme (JPND) as a project coordinator in 2015; a project founded by Fondazione Regionale per la Ricerca Biomedica (FRRB) in 2019; a Project founded by the European Center of Nanomedicine (CEN) as PI of the UNIMIB Unit in 2014, with the aim to design nanoparticles for human glioblastoma imaging and treatment. In 2013, she was a coordinator of a Privately funded Project (Fondazione Banca del Monte di Lombardia). In 2013, she was awarded of "63rd Lindau Nobel Laureate Meeting – Chemistry" and in 2018 she won Jorge Heller Outstanding Paper Award. During her trajectory, F.R. has been able to establish close collaborations with outstanding researchers from very diverse scientific backgrounds. She has been invited to give Ad Hoc seminars; her research work was presented in major conferences and contributed for attracting competitive funding from international agencies. In addition, F.R. has knowledge in drug discovery as she is co-inventor in 2 families of international patents and is Chief Operating Officer (COO)/Head of R&D of AmypoPharma S.r.l. (spin-off of UNIMIB). She has also teaching experience as lecturer in Biochemistry and Nanomedicine of graduate students and as tutor for students degree at UNIMIB. In summary, F.R. track record demonstrates an extended research experience and technical maturity (also proven by several articles where she appears as last author position) that allows her

to conduct future research with leadership and independent-thinking abilities (also proven by several articles where she appears without her PhD supervisor).

ABSTRACT. Cerebrovascular dysfunctions are a common feature of several neurodegenerative disorders, including Alzheimer's disease (AD). Increasing evidence describes impairment of the brain vasculature as an early event in AD, possibly caused by oxidative stress and responsible for cerebral blood flow reduction and blood-brain barrier (BBB) alterations, that culminate in neurodegeneration. Damage to the vascular endothelium is further induced by b-amyloid (Ab) peptides, a pathological hallmark of AD, toward the generation of reactive oxygen species (ROS) in endothelial cells. Therefore, oxidative stress has an important role in the pathophysiology and progression of AD. In this scenario, the use of cerium oxide nanoparticles (CNP) as ROS scavenging agents has gained increasing interest. Here we firstly investigated the ability of CNP to hinder ROS production by human cerebral microvascular endothelial cells (hCMEC/D3) exposed to Ab oligomers. The results showed that treatment with CNP restored basal ROS levels in brain microvascular cells both after acute or prolonged exposure to Ab. Then, we showed that the uptake of CNP increased after cell incubation with Ab. To gain insight into this phenomena, cell surface modifications were investigated under Ab treatment. We demonstrated that vascular pro-oxidant stimuli, i.e. cell exposure to Ab and hydrogen peroxide, induced microvilli-like protrusions on the surface of endothelial cells, which enhance CNP binding to the cell surface. This allows the possibility to exploit endothelial microvilli formation under oxidative stress conditions to boost the uptake of anti-oxidant nanoparticles at the vascular level as potential therapy for ROS-mediated cerebrovascular dysfunction in brain disorders.