5.2 EXPECTED OUTCOME OF THE GRAL PROJECT DESCRIBED IN SECTION 2.2.3

5.2.1 Molecular Machines and Dynamics

Expected results	
Virus host-pathogen interactions - Structural virology - Structure and dynamics of viral replication machines and transcriptional complexes - Structures of viral ribonucleoprotein assemblies - Virus budding and entry - Viral glycobiology and other post-translational modifications **Microbial host-pathogen interactions** - Structural characterization of bacterial cell wall elongation machineries - Sporulation - Structural and functional insight into protein interactions that can be targeted for the development of new antibiotherapies - New natural product inhibitors of cell wall formation in bacterial pathogens **- Bacterial nanomachines** - Key microbial metalloproteins - Antibiotic (bio)synthesis pathways - Novel drug targets against invasive fungal pathogens **Immunity and infection** - Innate immune factors - HIV immunogens - Therapeutic antibodies - C-type lectins receptors as target for infection or immune activation: Decoding Pathogen Surface Glycan recognition by the immune system. - Molecular organization of the efferosynapse **Membrane transport and signaling** - Structure and dynamics of transporters (phosphate transporter, toxoplasma, nucleotide transporter, rickettsia, rhodopsins etc) - Molecular mechanisms of neurotransmission (5-HT3 and receptors, GPCRs) - Identification of membrane protein targets of chemical disruptors - Mechanisms of receptor-dependent pore formation by secreted bacterial toxins	**Epigenetics and cancer** - Structure and function of epigenetic regulators (readers, writers, erasers) - Structure of the chromatin fiber and assembly intermediates - Structure and function of DNA repair machinery - Understanding assembly and function of cell division apparatus **New Methods** - Cryogenic and correlative nanoscopy - Application of time-resolved serial crystallography at synchrotrons and XFELs - New single molecule fluorescence approaches to study large and dynamic systems - New methodologies to study highly dynamic multi-component assemblies (combining super-resolution, smFRET, NMR, SAXS, AFM, EM) - New NMR methodologies to understand interaction mechanisms and dynamics of intrinsically disordered proteins - Micro electron diffraction, CLEM and super CLEM, high resolution electron tomography, cryo-FIB-SEM - Real time NMR - Solid state NMR of membrane proteins - Integrative modeling relating molecular structure and macroscopic morphology and localization. - Computational approaches to combine NMR, X-ray and EM data - Multiscale modeling methods to model complex biological processes (such as virus budding, filament assembly….)
	Global outcomes (restructuring)
	- Advanced methods development and application for biology - Fostering interdisciplinarity - Outreach to the Grenoble integrated structural biology community - Combine expertise of GRAL and ARCANE for drug design - Towards atomic-level description of a cell at high spatial and temporal resolution - Enabling biotechnology

5.2.2 Self-organization of living systems

Expected results	Global outcomes (restructuring)
Multi-cellular assemblies - Angiogenic network to feed organoids (O_2, energy, nutriments) - Fate of metals and chelating drugs liver mimicking spheroids. - Organoids as relevant surrogate models for organogenesis, pathogenesis and function of human organs - Organ-on-chips as biomimetic multicellular assemblies for drug screening and toxicity tests **Dynamics of protein complexes** - Control of genome expression by plant developmental regulators. - Protein-DNA and protein-RNA interactions in gene regulation and splicing - Interaction of transcriptional metallo-regulators with their DNA targets or anti-virulence drugs - Structure/function of novel metallo-proteins - Understanding the dynamic principles of cytoskeleton self-organization during morphogenesis. **Chloroplast functions and biogenesis** - Investigate limiting steps of photosynthetic electron transfer - Ion dynamics in cells and subcellular compartments - Dialog between light perception and photosynthesis and CO_2 metabolism. - Role of DNA and RNA methylation in the microalgae acclimation to stresses **Dynamics of subcellular architectures** - Rules for the self-assembly of lipids into membranes - Lipo-protein supercomplexe dynamics - Organelles imaging *in cellula* (FIB-SEM; cryo-EM tomography) and dynamic behavior *in vivo* (SANS) - Trafficking and fate of metal ions in cells	- Structuring the UGA community around self-assembly at various levels (molecules, cells, and organism). Strong link with the IAB laboratory for lipid and cell assemblies. Potential to develop a connection with social science (PACTE laboratory/ A-L Amilhat Szary, human auto-organization) - Combine structural knowledge with new genome editing tools to control plant traits and photosynthesis/CO_2 capture - A holistic view of photosynthesis - Combine expertise in GRAL and ARCANE to propose new solutions for artificial photosynthesis, solar fuel production or CO_2 sequestration. - Unravel general rules governing assembly and dynamics of cellular and subcellular structures - Use of organ surrogates for basic biology, drug screening, regenerative medicine and limit animal testing