0000000254 - PHOTO_SWITCH

PhD Research and Training proposal

1. EXCELLENCE (4 pages max)

1.1. Pre-proposal's context, positioning and objectives

Hypothesis and objectives

An evolutionarily conserved molecular switch mediated by the interaction between the TOR kinase subunit LST8 and the intrinsically disordered N-terminal region (NTR) of RSH3 coordinates chloroplast activity (photosynthesis) with cytoplasmic TOR signalling.

Objective 1: Characterize the molecular basis of the TOR-RSH3 switch
Objective 2: Determine the functional role of the TOR-RSH3 switch

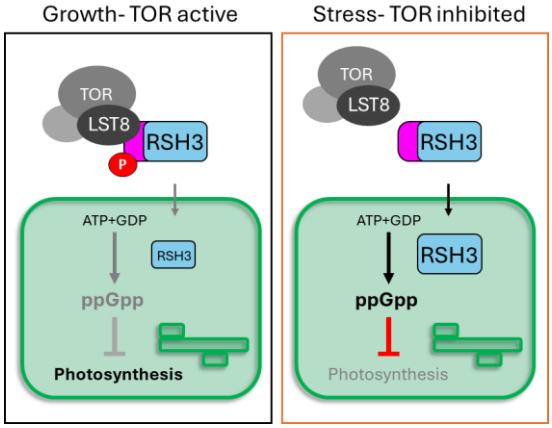

Figure 1. A TOR–RSH3 regulatory switch coordinating chloroplast ppGpp signalling and photosynthesis. When TOR is active and promoting growth (left), the TOR subunit LST8 associates with the intrinsically disordered N-terminal region of RSH3 (magenta) and promotes TOR-dependent phosphorylation (P), thereby limiting RSH3 accumulation in chloroplasts. Upon TOR inhibition or stress (right), RSH3 phosphorylation is lost and the protein accumulates in chloroplasts, increasing ppGpp levels and down-regulating photosynthetic activity. The molecular and structural basis of this TOR–RSH3 switch remains unknown and constitutes the central objective of the PHOTO_SWITCH project.

Context and positioning

Cellular growth in eukaryotes is regulated by complex signalling networks that integrate nutrient availability with the core machinery of proliferation. At the centre of this regulation is TOR (Target of Rapamycin), a conserved Ser/Thr kinase complex that acts as a master regulator, processing inputs from nutrients, energy, and hormones to balance anabolic and catabolic pathways to coordinate growth across diverse eukaryotes. While TOR's role in cytoplasmic growth regulation is well-established (Liu *et al.*, 2025), its role in coordinating cytoplasmic activity with chloroplast function- especially photosynthesis - has only recently emerged as a research focus (Crespo *et al.*, 2025). Photosynthesis, the process by which plants convert sunlight into chemical energy, underpins all life on Earth by producing oxygen and organic compounds that fuel food chains. Understanding how TOR modulates photosynthesis is not only fundamental to plant biology but also critical for developing strategies to enhance crop resilience and mitigate the impacts of climate change.

The BIAM-LGBP pioneered the discovery that TOR regulates photosynthesis by controlling the accumulation of ppGpp, a nucleotide second messenger that inhibits plastid gene expression and photosynthesis (Mehrez *et al.*, 2023; D'Alessandro *et al.*, 2024). Originating from studies in bacteria, where ppGpp is produced during nutrient stress and serves as an allosteric and GTP-competitive inhibitor impacting numerous enzymes (Irving *et al.*, 2021; Bange *et al.*, 2021), the role of this signalling molecule is an emerging theme in plant biology. Our laboratory has been at the forefront of research on ppGpp in plants, and along with others we have revealed a pivotal role for ppGpp in plant adaptation, where it influences plant size, senescence, nitrogen limitation responses, and pathogen interactions (Maekawa *et al.*, 2015; Sugliani *et al.*, 2016; Abdelkefi *et al.*, 2018; Goto *et al.*, 2022; Romand *et al.*, 2022, 2025; Li *et al.*, 2022). ppGpp is now widely considered a down-regulator of plastid gene expression, which is likely how it regulates photosynthesis (Maekawa *et al.*, 2015; Sugliani *et al.*, 2016; Romand *et al.*, 2022; Ito *et al.*, 2022).

The biosynthesis and degradation of ppGpp, crucial for its cellular levels and effects, are facilitated by the nucleus-encoded chloroplastic RelA SpoT Homolog (RSH) enzymes. These enzymes are often bi-functional, catalysing both the synthesis of ppGpp and its hydrolysis, and respond to stress stimuli at the transcriptional and post-transcriptional levels (Romand *et al.*, 2022; D'Alessandro *et al.*, 2024). In the model plant Arabidopsis, three

conserved RSH enzyme families - RSH1, RSH2/3, and RSH4/CRSH - play distinct roles, with RSH2 and RSH3 primarily synthesizing ppGpp and RSH1 acting as the main hydrolase (Avilan *et al.*, 2019; Mehrez *et al.*, 2023).

TOR negatively regulates the accumulation of ppGpp by directly targeting RSH3 in the cytosol. The TOR subunit LST8 (lethal with SEC13 protein 8) interacts with the intrinsically disordered N-terminal region (NTR) of RSH3(D'Alessandro *et al.*, 2024). This interaction functions as a dynamic molecular switch: when TOR is active, LST8 binds the RSH3 NTR, promotes its TOR-dependent hyperphosphorylation, and prevents its import into chloroplasts, thereby limiting ppGpp accumulation and sustaining photosynthesis. Conversely, TOR inhibition releases this brake, allowing RSH3 to enter chloroplasts, accumulate ppGpp, and downregulate photosynthesis. This switch-like mechanism enables plants to rapidly coordinate cytoplasmic TOR signalling with chloroplast activity in response to environmental cues.
However, the structural and biochemical basis of the TOR-RSH3 switch- specifically how LST8 recognizes and binds the intrinsically disordered NTR of RSH3- remains unknown. To address this, PHOTO_SWITCH will employ an interdisciplinary approach, combining structural biology (led by Dr. Chloé Zubieta at LPCV, an expert in protein structure) to characterize the LST8-NTR interaction; biochemistry to dissect the regulatory mechanisms of the interaction (CZ, BF); and plant physiology to validate its functional consequences in vivo (BF). This project will leverage our expertise in ppGpp and chloroplast biology alongside Dr. Zubieta's cutting-edge structural biology and experience with intrinsically disordered proteins (Jung *et al.*, 2020; Hutin *et al.*, 2023; Hu *et al.*, 2024; Alberti *et al.*, 2025) to elucidate this critical regulatory switch. Functional interpretation of TOR-dependent regulation will be supported by targeted quantitative ppGpp measurements performed with the Nicolaus Copernicus University partner (Poland)(Turkan *et al.*, 2024), ensuring rigorous linkage between molecular mechanism and metabolic outcome.

Methodology

Work Package 1: Characterizing the Molecular Basis of the TOR-RSH3 Interaction

Work Package 1 will focus on structural and biochemical characterisation, building on the expertise of the LPCV in structural biology and intrinsically disordered proteins.

1a. Optimise expression and purification of proteins.

- Preliminary tests show that *E. coli* expression does not produce soluble protein under a number of different conditions for either LST8 or RSH3 NTR, likely due to the disordered nature of the NTR and potential toxicity of LST8 overexpression. Denaturation (i.e. 8M urea) and refolding protocols will be tested for the NTR of RSH3. The Zubieta team routinely purifies intrinsically disordered proteins under denaturing conditions followed by urea depletion for downstream biochemical and structural studies.
- The student will test and optimise production of recombinant Arabidopsis LST8 and the RSH3 NTR in eukaryotic expression systems (insect and mammalian cells) and cell free expression systems established in the LPCV. Co-expression of LST8 with the NTR of RSH3 will also be performed to stabilize the RSH3 fragment. The insect system is expected to yield soluble LST8, as seen for human LST8 which is commercially produced in Sf9 insect cells (BPS Bioscience).

1b. X-ray crystallography of LST8

- LST8 is a 7-bladed WD40 β-propeller protein, a fold known for its structural rigidity and crystallization propensity. Furthermore, mammalian and yeast LST8 structures have been solved by X-ray crystallography and cryo-EM, often in complex with other TOR components (https://www.rcsb.org/structure/4JSX), suggesting the Arabidopsis LST8 is an attractive and feasible structural target the would provide an anchor for stabilizing the interaction with the disordered RSH3 NTR..
- We will co-crystallize LST8 with the NTR of RSH3 (WP1a) and/or synthetic peptides representing the minimal interaction domain of RSH3-NTR (identified via modelling approaches, below). These complementary approaches leverage the ordered nature of LST8 to stabilize the interaction with the flexible NTR of RSH3 and facilitate structural studies.

- If co-crystallization fails, we will use soaking experiments to bind peptides to crystallized LST8.
- Cryo-EM offers an alternative strategy for atomic resolution structural characterization, although the small size of the complex would require technical optimization (phase plates to improve contrast).

1c. Alternative structural approaches for the LST8-RSH3 NTR complex

- Small-Angle X-ray Scattering (SAXS) experiments will provide low-resolution structural information about the shape, size, and flexibility of the LST8-RSH3 NTR complex in solution. Extensive ordering of the RSH3 NTR may be characterized using this solution state technique (BM29, ESRF, Dr. Mark Tully collab.).
- Cross-linking mass spectrometry (XL-MS) will be performed to map the interactions between LST8 and RSH3 NTR. The Zubieta team collaborates with mass spectrometry experts and has access to an on-site mass spectrometry platform (EDyP, CEA, Grenoble).
- NMR titration experiments using 15N isotope labelling of the RSH3 NTR and unlabelled LST8 will be performed, recording H^{1}-N^{15} HSQC spectra.

1d. Computational Modeling

- We will use AlphaFold3 AI and docking software including Rosetta and HADDOCK to predict the LST8-RSH3 NTR interaction interface and guide experimental design.
- Molecular dynamics (MD) simulations will help explore the conformational space of the NTR and its interaction with LST8, providing insights into binding kinetics and allostery.
- Time-permitting, this approach could be extended to analyzing the evolution of the LST8-RSH3 NTR interaction region across land plants.

1e. Interaction mapping, mutagenesis and binding affinity

- Previous work has established the LST8–RSH3 interaction by yeast two-hybrid assays (D'Alessandro *et al.*, 2024). This system will be used to assess the impact of targeted mutations at the predicted interaction interface, as well as a randomly mutagenised library of RSH3-NTR variants generated by mutagenic PCR. Together, these approaches will enable the identification of residues critical for complex formation and guide subsequent structural and biophysical analyses.
- Purified LST8 and the full RSH3 NTR or peptides, and mutated version, will be used in isothermal titration calorimetry (ITC) and microscale thermophoresis (MST) experiments to quantify binding affinity (Kd).

Work Package 2: Determining the Functional Consequences of the TOR-RSH3 Interaction

Work Package 2 will address in vivo functional validation in plants, supported by physiology at BIAM-LGBP physiology and quantitative ppGpp analysis at NCU.

2a. Chloroplast import and phosphorylation.

- Chloroplast import and phosphorylation can be conveniently studied by transient expression in *Nicotiana benthamiana* leaves (D'Alessandro *et al.*, 2024).
- RSH3-NTR fluorescent protein fusion variants generated in WP1 will be expressed and analysed for altered phosphorylation by Phos-Tag SDS PAGE, and LC-MSMS following immunoprecipitation.
- Chloroplast import will also be assessed by quantifying the ratio of pre-protein to mature imported protein by immunoblots and quantitative fluorescence microscopy.

2b. Generation of Arabidopsis RSH3-NTR variant lines.

- We will generate Arabidopsis lines expressing full length RSH3 with different NTR variants (e.g. no LST8 interaction as identified in WP1, phosphodead and phosphomimic variants).
- These lines will be generated by
    - classic TDNA insertion in ppGpp-null CRISPR mutants lacking *RSH2*, *RSH3*, and *CRSH* that we recently isolated in the lab
    - a cutting edge CRISPR knock-in system to modify the NTR of the native RSH3 protein directly on the chromosome that we are currently setting up in the lab (Schreiber *et al.*, 2024).

2c. Physiology of mutants with an altered TOR-RSH3 switch.

- The RSH3-NTR variant plants generated above will be tested for growth and photosynthetic phenotypes, RSH3 protein levels, and alterations in ppGpp accumulation.
- RSH3-NTR variant mutants will then be tested as above under varying stress conditions known to affect ppGpp signalling such as under nitrogen deprivation conditions, high-light and interactions with pathogens. A number of new conditions are being identified in undergoing projects in the lab, and these could also be integrated into the assays.

Originality and innovative aspects of the planned research

The PHOTO_SWITCH project stands out due to its unique combination of structural, biochemical, and physiological approaches to address a fundamental gap in plant biology.

First, it will provide the first structural characterization of the interaction between the TOR subunit LST8 and the intrinsically disordered N-terminal region of RSH3. While the role of TOR in regulating ppGpp and photosynthesis is established, no structural data currently exists for this interaction. We will use LST8's structured WD40 β-propeller domain as an anchor to stabilize the disordered NTR, employing X-ray crystallography of LST8-peptide complexes, cryo-EM for full-length complexes, and complementary structural approaches if needed such as SAXS and NMR to study protein-protein interactions in solution and their dynamics.

Second, the project integrates three complementary disciplines: structural biology to resolve the LST8-RSH3 NTR interaction, in vivo and in vitro biochemical assays to quantify binding affinity of WT and mutants, and plant physiology to validate the functional role of this interaction in Arabidopsis mutants in the appropriate background. This convergence is rare in plant biology and aligns with SCHADOC's emphasis on interdisciplinarity.

Third, the focus on intrinsically disordered regions represents a methodological challenge. The NTR of RSH3 is a dynamic IDR, and our integrated approach—combining AlphaFold3 modeling, molecular dynamics simulations, and experimental structural techniques—will capture its functional conformations and define its binding motifs.

Finally, understanding the TOR-RSH3 switch could enable targeted modulation of photosynthesis and stress responses in crops through weakening or strengthening the LST8-RSH interaction. For example, manipulating this interaction might improve drought tolerance or nutrient-use efficiency, addressing key agricultural challenges under climate change. By linking TOR signalling to the regulation of photosynthetic energy metabolism through a structurally defined molecular switch, PHOTO_SWITCH reveals a previously unrecognised regulatory paradigm in plant energy signalling.

1.2. Interdisciplinary dimension of the project

The PHOTO_SWITCH project integrates three complementary disciplines to address a question inaccessible to any single field. **Structural biology** (LPCV, Dr. Zubieta) will resolve the LST8-RSH3 NTR interaction using X-ray crystallography, or complementary structural techniques as appropriate such as cryo-EM, NMR, SAXS and XL-MS, leveraging LST8's ordered WD40 domain to stabilize the disordered NTR. **Biochemistry** (LGBP/LPCV) will quantify binding affinities of WT and mutant proteins (ITC/MST) and map the interaction by Y2H. In vivo phosphorylation (Phos-Tag SDS-PAGE) will be performed. Taken together these studies will bridge structure and in vivo function. **Plant physiology** (LGBP) will validate in vivo consequences using Arabidopsis mutants, with NCU partners contributing ppGpp measurements under stress conditions.

This synergistic approach ensures true interdisciplinarity through:

- Shared objectives across all work packages
- Regular cross-disciplinary meetings to refine hypotheses
- Training of a PhD student in structural biology (LPCV/ESRF), targeted quantitative metabolite analysis (NCU, Poland), and plant physiology (LGBP)
- Development of a holistic model connecting atomic structures to whole-plant responses

This co-supervision structure ensures genuine interdisciplinary integration, training the PhD candidate at the interface of structural biology, quantitative biochemistry, and plant physiology.

2. IMPACT (2 pages max)

2.1. Expected impact of the project on the candidate's career

PHOTO_SWITCH will provide the doctoral candidate with a uniquely interdisciplinary training at the interface of structural biology, quantitative biochemistry, and plant physiology. Through training spanning recombinant protein production, synchrotron-based structural analysis, targeted ppGpp quantification by LC-MS/MS, and in vivo functional validation in plants, the candidate will acquire a unique combination of conceptual and technical competences that are highly valued in both academic and non-academic research environments.

International co-supervision and secondments at LPCV/ESRF and Nicolaus Copernicus University will strengthen scientific autonomy, project management capacity, and experience in multicultural research settings. Training in open science practices, data stewardship, and reproducible research will further enhance the candidate's professional profile in line with European research standards. Complementary institutional and international training opportunities, including the IM2B *Plinius* programme and EMBO practical courses, will further strengthen transferable and interdisciplinary competences.

Together, these elements will prepare the candidate for diverse career paths, including academic research in plant biology or structural biology, positions in agri-biotechnology or analytical sciences, and roles related to research management, innovation, or science policy. By combining high-level scientific expertise with transferable skills such as interdisciplinary communication, international collaboration, and responsible research practices, PHOTO_SWITCH will substantially enhance the fellow's long-term career prospects.

2.2. Expected impact for the thematic axis

PHOTO_SWITCH directly addresses the SCHADOC thematic axis related to climate change and environmental challenges by elucidating molecular mechanisms that enable plants to balance growth with stress adaptation. Understanding how the TOR–RSH3 regulatory switch modulates photosynthesis and energy allocation under adverse conditions will advance fundamental knowledge of plant stress biology while also identifying potential strategies to improve crop resilience to drought, nutrient limitation, and fluctuating environments.

Scientifically, the project will deliver the first integrated structural, biochemical, and physiological characterisation of this regulatory switch, thereby opening new conceptual frameworks for studying intrinsically disordered-proteins, chloroplast-cytoplasm communication and ppGpp signalling in plants. Methodologically, the combination of advanced structural approaches, quantitative metabolite analysis, and functional plant biology exemplifies the interdisciplinary innovation promoted by SCHADOC.

Beyond academia, the knowledge generated may inform future strategies in crop improvement, sustainable agriculture, and climate-resilient food production. Stakeholders potentially benefiting from these advances include plant scientists, breeding programmes, agri-biotechnology companies, and policy actors concerned with food security and environmental sustainability. These advances directly support European priorities in sustainable agriculture, climate adaptation, and food security under the Green Deal and Farm-to-Fork strategies.

2.3. Dissemination, exploitation and communication activities planned

Dissemination will follow a strong open science approach. Scientific results will be published in peer-reviewed open-access journals, with supporting data and datasets deposited in appropriate specialist repositories ((e.g., Protein Data Bank, SASBDB, PRIDE) as well as in national open repositories such as data.gouv.fr (Field, 2025), ensuring persistent identifiers, FAIR compliance, and long-term accessibility. High-impact findings will additionally be targeted to broad-scope international journals to maximise scientific visibility.

The doctoral candidate will receive structured training in scientific writing and presentation, with opportunities to present results at national meetings (e.g., the French Society of Plant Biology and Photosynthesis community meetings) and major international conferences, thereby strengthening professional visibility and networking.

Exploitation of results will primarily concern conceptual and methodological advances relevant to plant stress adaptation and crop resilience. Where appropriate, opportunities for intellectual property protection and

collaboration with agri-biotechnology stakeholders will be evaluated in line with institutional policies, building on existing patenting experience within the supervisory team (Field *et al.*, 2021).

Public engagement will include participation in major outreach initiatives such as the Fête de la Science, AMU-organised “speed-searching” interactions with the public, and CNRS “Visites insolites” laboratory open-days. Additional activities may involve presentations to school and university audiences and contributions to institutional communication channels such as via institutional and researcher social media accounts (Bluesky, LinkedIN) and written up as articles in institutional magazines for the general public and specialists e.g. Les Defis du CEA, and Le Journal of the CNRS or institution newsletters.

Together, these actions will promote awareness of plant science, climate challenges, and research careers, ensuring societal impact alongside scientific dissemination.

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3. IMPLEMENTATION (2 pages max)

Work plan and task integration

PHOTO_SWITCH is organised into two interconnected work packages (WPs) designed to achieve all scientific and training objectives within 36 months. Continuous interaction between structural, biochemical, and physiological approaches is ensured through shared milestones at months 12, 24, and 36.

Organisation and supervision structure

The project will operate under an integrated international co-supervision framework.

Ben Field (BIAM-LGBP) will coordinate the project and supervise plant physiology, ppGpp signalling, and in vivo validation, bringing established leadership in chloroplast signalling and TOR–ppGpp regulation together with access to advanced plant growth, biochemical, and biophysical platforms ensuring robust functional validation of structural findings.

Chloé Zubieta (LPCV) will co-supervise structural and biophysical investigations, including recombinant protein production, crystallography, SAXS/cryo-EM, , data processing, structure building and validation. Chloé Zubieta leads the StrucDev team at LPCV and brings internationally recognised expertise in the structural and biophysical analysis of intrinsically disordered regulatory proteins, a central aspect of the LST8–RSH3 interaction. Her laboratory's immediate proximity to the European Synchrotron Radiation Facility (ESRF) and established access to crystallographic and SAXS beamlines significantly strengthen the feasibility and efficiency of the structural work package.

The Nicolaus Copernicus University (NCU, Poland) partner lead by Dr. Milena Kulasek will co-supervise targeted ppGpp quantification by LC-MS/MS and support quantitative biochemical interpretation.

Supervisors will jointly define milestones, evaluate progress, and mentor the PhD candidate through regular trilateral meetings, ensuring full interdisciplinarity and international integration.

PHOTO_SWITCH project timeline	Year 1		Year 2		Year 3	
	0 - 6	6 - 12	12 - 18	18 - 24	24 - 30	30 - 36
WP1 Structural & biochemical mechanism						
Protein production, interaction mapping, first biophysics						
Structural characterisation & modelling						
Quantitative biophysics & variant selection						
WP2 Functional validation in plants						
Transient functional validation (*N. benthamiana)*						
Arabidopsis edited/variant lines generation						
Physiology & ppGpp quantification						
Stress biology, integration, publication						
Mobilities and outputs						
LPCV / ESRF 1 (3 months)		X				
LPCV /ESRF 2 (3 months)			X			
NCU (1 month)				X		
Manuscript and thesis preparation						

Structured training and mobility

The PhD programme combines local research with targeted international secondments:

- **LPCV/ESRF (2 × 3 months):** structural biology, protein production, crystallography, SAXS, and synchrotron analysis.
- **NCU Poland (1 month):** LC-MS/MS ppGpp quantification and quantitative biochemical analysis.

Each secondment includes defined learning objectives, joint supervision, and formal progress evaluation.

In addition to the training opportunities provided by SCHADOC and the doctoral school, the PhD candidate will benefit from the IM2B institute's doctoral training programme Plinius, which offers a broad portfolio of relevant courses covering both technical and transferable skills (https://pliniuscursus.univ-amu.fr/programm/list-of-trainings/). The candidate will also have access to specialised international training schools of one to two weeks' duration, such as the EMBO Practical Course on the Structural Characterization of Macromolecular Complexes and EMBO courses dedicated to small-angle scattering.

Project coordination and monitoring

Monthly meetings will track progress and adjust strategy, complemented by formal milestone reviews at months 12, 24, and 36 assessing scientific results, training, and career development. This governance ensures feasibility within 36 months and high-quality interdisciplinary mentoring.

Resources and infrastructure

PHOTO_SWITCH relies on complementary expertise in plant signalling (BIAM-LGBP), structural biology (LPCV), and targeted quantitative metabolite analysis (NCU). Together, these environments provide the facilities, supervision, and international training required to achieve all objectives within the doctoral timeframe.

Planned mobility periods at LPCV/ESRF and Nicolaus Copernicus University are fully compatible with the SCHADOC doctoral funding framework, as associated costs are limited to travel, accommodation, and subsistence while access to major research infrastructures and analytical platforms is provided in kind by the host institutions. Complementary resources further strengthen feasibility, including competitive ESRF beamtime programmes providing instrumentation, technical support, and training; externally funded advanced courses (e.g., EMBO practical training and the IM2B *Plinius* doctoral programme); and ongoing ANR-funded projects within BIAM-LGBP and LPCV that supply established experimental platforms, consumables, and technical expertise. Together, these elements ensure that the scientific objectives, international mobility, and training activities of PHOTO_SWITCH are fully achievable within the doctoral funding framework.

Open science strategy

All data will follow FAIR principles and be stored on secure CNRS servers, with processed datasets deposited in public repositories (i.e. PDB, MetaboLights, DATAMU). Results will be disseminated via preprints and open-access publications, supported by electronic laboratory notebooks ensuring reproducibility. Open science practices will form part of doctoral training through hands-on experience in data management, sharing, and transparent publication, maximising scientific and societal impact.

Risk mitigation

Key risks are mitigated through complementary strategies.

- Protein expression challenges will be addressed using prokaryotic and eurkaryotic expression systems, codon optimisation and rational construct design based on domain boundaries and predicted protein-protein interaction interfaces.
- Structural determination risks are mitigated through a multi-method strategy in which crystallography represents only one of several complementary approaches. Solution-state techniques including SAXS and NMR and cross-linking mass spectrometry, together with AlphaFold-guided modelling and quantitative biophysics, will provide robust mechanistic insight even in the absence of well-diffracting crystals of LST8-RSH3. This integrated framework ensures that WP1 can deliver publishable structural and functional conclusions independently of any single technique.
- Delays in Arabidopsis mutant generation will be offset by rapid transient assays in *Nicotiana benthamiana*, while functional and ppGpp analyses in plants remain independent of high-resolution structures. This design avoids a single point of failure that could jeopardise the student's PhD trajectory.
- Synchrotron constraints will be managed through advance scheduling and alternative techniques.

These measures ensure scientific deliverables, interdisciplinary training, and completion within 36 months.

4. ETHICS SELF-ASSEMENT

The PHOTO_SWITCH project involves molecular biology, biochemistry, structural biology, and experimentation with genetically modified plants. No activities involving human participants, human biological material, personal data, or animal experimentation are foreseen.

Laboratory work will follow institutional health and safety regulations governing the handling of chemicals, biological materials, and specialised equipment. Personnel will receive mandatory safety training and will use appropriate engineering controls and personal protective equipment. Experiments performed at synchrotron facilities will comply fully with facility-specific radiation protection procedures, safety training requirements, and controlled-area regulations.

Generation and cultivation of genetically modified Arabidopsis lines will be conducted exclusively within authorised GMO containment installations and in accordance with applicable national and institutional biosafety regulations, including controlled access, traceability, and approved waste disposal.

All project partners will comply with relevant EU and national ethical, biosafety, and safety frameworks, and any required authorisations will be obtained prior to the corresponding experimental activities.

5. REFERENCES

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