



PhD Research Proposal Form China Scholarship Council (CSC) - ENS Group

FIELD: ----BIOLOGY-----

Thesis subject title:

Investigation of the TCTP pathway controlling cell proliferation and organ growth

Name of the French doctoral school : Biologie Moléculaire Intégrative et Cellulaire, BMIC-ED340

Name of the Research team : Flower Morphogenesis team, Reproduction et Développement des
Plantes laboratory

Website : <https://www.ens-lyon.fr/RDP/Morphogenese-florale/>
<https://www.ens-lyon.fr/RDP/>

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Lab Language : English

Research Proposal Abstract :

Investigating cell cycle regulation is essential in basic and applied sciences, as its perturbation can lead to deleterious defects, or very positive in the case of biomass production. We previously discovered that the TRANSLATIONALLY CONTROLLED TUMOR PROTEIN (TCTP) is a major regulator of cell proliferation and growth in plants. Controlled translation of TCTP limits its accumulation to dividing cells and its overaccumulation leads to accelerated growth (Brioude et al., 2010; Betsch 2017). Recently, we showed that TCTP interacts with the COP9 signalosome subunit CSN4 to promote cell proliferation through the modulation of protein ubiquitination/degradation (Betsch et al., 2019; Xu et al., in preparation).

The aims of this PhD project will be to investigate how TCTP translation and accumulation is regulated, how TCTP/CSN4 controls cell proliferation and growth using *Arabidopsis* as model plant.

In a first part of the work, the PhD student will investigate how TCTP translation and accumulation is regulated. We aim to identify and functionally characterize the factors involved in the regulation of TCTP translation in order to restrict its accumulation to highly dividing cells. We have set up a genetic screen in *Arabidopsis* that has identified two mutant lines in which TCTP accumulates in all tissues. Recently we identified mutations in candidate genes likely associated with the observed TCTP-GFP over-accumulation. The PhD student will confirm that the identified mutated genes are associated with the observed TCTP protein accumulation in all tissues. The PhD student will then perform functional studies to validate the role of the identified candidate genes in the regulation of TCTP accumulation. To achieve this goal, functional complementation experiments and analyses of mutant lines deficient for the identified genes, will be performed.

In a second axis of TCTPATH project, we will unravel the mechanisms by which TCTP and its interacting factor (CSN4) control cell cycle progression and growth in *Arabidopsis*. The PhD student will explore the downstream events by which TCTP/CSN4 controls cell cycle progression in *Arabidopsis*. To identify the downstream targets of TCTP/CSN4, we are using a combination of a 'hypothesis-driven approach' by analyzing core cell-cycle regulators well known to be controlled by ubiquitin-dependent proteolysis, and an

unbiased approach (proteomics and transcriptomics) to unravel the gene and protein networks acting downstream of TCTP/CSN4.

The outcomes of this project are expected to bring novel and original research data of general scientific interest that we will continue reporting in high impact peer reviewed scientific journals. Importantly, the outcomes of this project are also expected to reach beyond *Arabidopsis* research as increased accumulation of TCTP in plants leads to enhanced growth. Therefore, the gained knowledge may be important in improving crops development.

We have already a candidate (Ms. Ying LIU) from a laboratory with whom we (at ENS de Lyon) have established an International Associated Laboratory (LIA HortiLab), directed by M. Bendahmane on the ENS/French side.

References :

- Betsch L, Savarin J, Bendahmane M*, Szécsi J* (2017) Roles of the Translationally Controlled Tumor Protein TCTP in Plant Development. [Results Probl Cell Dif](#) **64**,149-72.
- Betsch L, Boltz V, Brioude F, Pontier G, Savarin J, Wipperfurth B, Chambrier P, Girard V, Tissot N, Benhamed M, Mollereau B, Cécile Raynaud C, Bendahmane M*, Szécsi J* (2019) TCTP and CSN4 control cell cycle progression and development by regulating CULLIN1 neddylation in plants and animals. [PLoS Genet](#) **15**, e1007899.
- Brioude F, Thierry A-M, Chambrier P, Mollereau B, Bendahmane M* (2010) Translationally controlled tumor protein is a conserved mitotic growth integrator in animals and plants [PNAS](#) **107**, 16384-16389.

Type of PhD :

1.Full PhD

- Joint PhD/cotutelle (leading to a double diploma) : ~~YES~~ or NO
- Regular PhD (leading to a single French diploma) : YES or ~~NO~~

2. Visiting PhD (for students enrolled at a Chinese institution who will be invited to a French institution to carry out a mobility period) : ~~YES~~ or NO