FFG
Promoting Innovation.

STRIKING SYNERGIES: TOWARDS A COMPETITIVE ERC SYNERGY GRANT PROPOSAL

13 June 2023, FFG Academy

SYNERGY GRANT IN SHORT

- Supports groups of 2 - 4 Principal Investigators (PIs) and their teams to bring together skills, knowledge, and resources in order to jointly address ambitious research problems
- Open for all areas of research

Transformative research

- Should enable substantial advances at the frontiers of knowledge, stemming, for example, from the cross-fertilisation of scientific fields, from new productive lines of enquiry, or new methods and techniques, including unconventional approaches and investigations at the interface between established disciplines.

- Should have the potential of becoming a benchmark on a global scale

2 – 4 Principal Investigators (PI)
= Synergy Grant Group

+

Host Institution/s (HI)

including 1 Corresponding PI
(admin. contact for ERC)

Corresponding HI in EU-27 or Associated Countries
1 HI can be located outside of EU/AC

- Innovative and actives PIs in all career stages (no formal eligibility criteria), competitive track records as appropriate according to career stage
- Max. **EUR 10 million for up to 6 years** (up to EUR 14 million in defined exceptional cases)

- Minimum 30% time commitment to project by each PI
- Minimum 50% of total working time spent in EU-27 or a country associated to Horizon Europe AC by each PI, except for the case of one PI (not Corresponding PI) being located at a HI outside EU-27/AC

SYNERGY PROPOSAL STRUCTURE AND EVALUATION STEPS – INCLUDING PLANNED CHANGES

STEP 1

Extended Synopsis (B1) - 5 pages
+ CV and Track record - 4 pages per PI

Only B1 is evaluated at step 1

Panel Members – **Generalists** (1 Panel, ~ 85 members)

STEP 2

Research proposal (B2) - 15 pages
+ Resources section: no page limit

B1 and B2 are available to reviewers in step 2

cut-off: 7 times the panel budget

5 Panels á ~17 members
+ Remote Referees – **Specialists**

STEP 3

Interview with Panel
(with all PIs, in Brussels)

cut-off: 4 times the panel budget

TAILOR-MADE EVALUATION PROCESS
PLANNED CHANGES

Panel Members: Generalists
Step 1: **1 panel**, ~ 85 panel members
min. 3 Panel Members read B1
evaluation outcomes: A invited/A not invited, B, C

Step 2
5 panels formed dynamically (**2 PE-, 2 LS-, 1 SH-oriented**)
Panel Members & Remote Referees read B1 + B2
evaluation outcomes: A, B

Step 3
5 panels, composition may be changed again for **interview with all PIs**
evaluation otucomes: A, B

SCIENTIFIC EXCELLENCE: EVALUATION QUESTIONS INCLUDING PLANNED CHANGES (1)

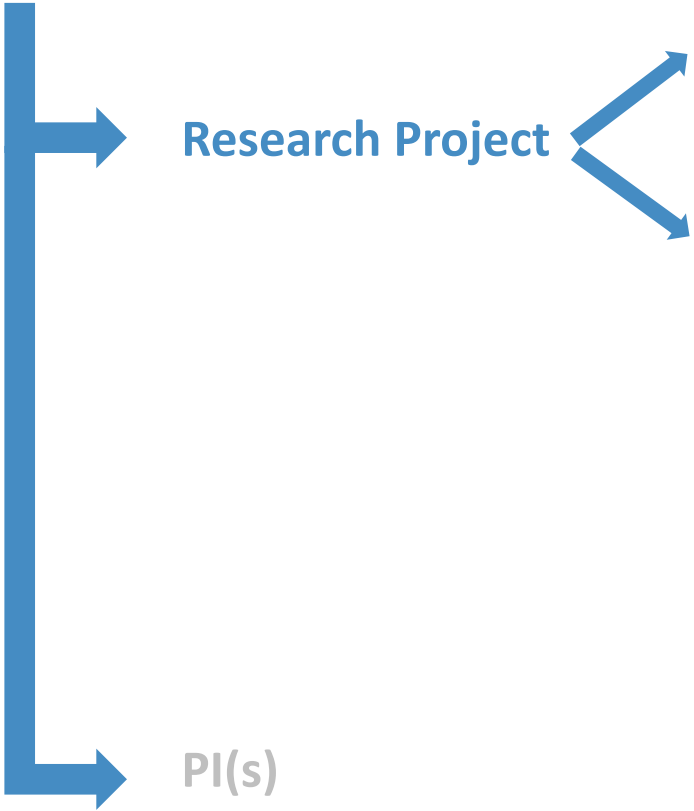
Research Project

Primarily: ground-breaking nature, ambition, feasibility

PI

At the same time: intellectual capacity, creativity, commitment; focus: required scientific expertise and capacity

SCIENTIFIC EXCELLENCE: EVALUATION QUESTIONS INCLUDING PLANNED CHANGES (2)



Ground-breaking nature and potential impact of the research project: important challenges? ambitious & beyond state of the art? ~~high risk/high gain?~~

Scientific approach: feasible? methodology & working arrangements appropriate? ~~novel methodology~~? adequate timescales, resources, PI commitment?

Going beyond what PIs could achieve alone?

Combination of scientific approaches that are crucial to address the scope and complexity of the research questions to be tackled ?

SCIENTIFIC EXCELLENCE: EVALUATION QUESTIONS INCLUDING PLANNED CHANGES (3)

PI(s)

- demonstrated ability to conduct ground-breaking research?
- evidence of creative and original thinking?
- required scientific expertise and capacity?

- Synergy Grant Group: To what extent does the Synergy Grant Group successfully demonstrate in the proposal that it brings together the know-how – such as skills, experience, expertise, disciplines, teams – necessary to address the proposed research question (based on the Extended Synopsis)?

WHAT MAKES AN ERC “PROFILE“?
PLANNED CHANGES

STARTER

Should have already shown **evidence of the potential for research independence**, E.g. by having produced at least **one important publication as main author** or without the participation of their PhD supervisor

CONSOLIDATOR

Should have already shown **evidence of research independence.**

ADVANCED

established research leaders, recognised track record of research achievements

PRESENTING THE PIS IN THE PROPOSAL
PLANNED CHANGES

- **CV & Track Record, up to 4 pages:**

– personal details, education, key qualifications, current position(s) and relevant previous positions,

– list of up to ten research outputs; emphasis on more recent achievements,

– list of selected examples of significant peer recognition

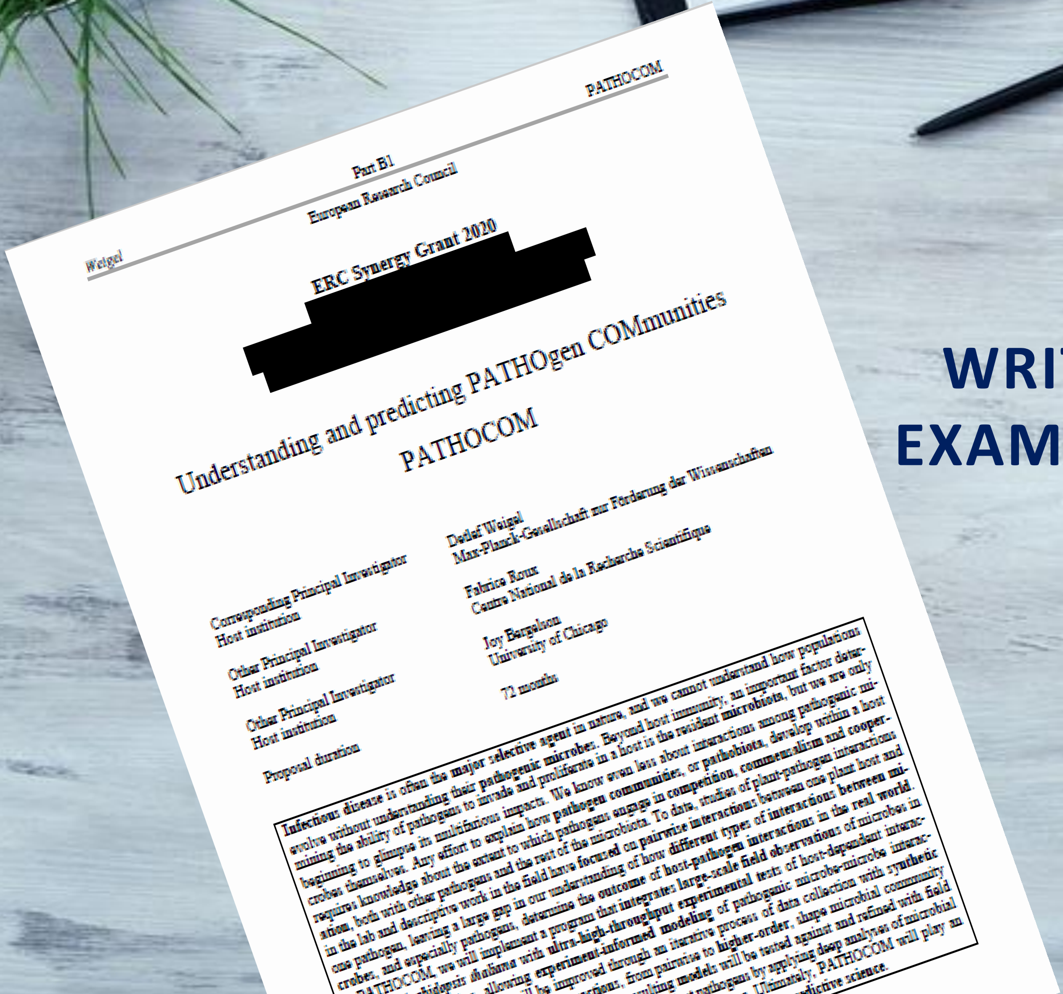
– short explanation of significance of selected outputs and role of applicant

– optional: information on career breaks, diverse career paths – to provide context to the evaluation panels

- **Extended Synopsis (B1) and Scientific Proposal (B2):**

– e.g. references: As we could show in [ref],…

– preliminary results


Weigel

Part B1

European Research Council

PATHOCOM

ERC Synergy Grant 2020

[redacted]

Understanding and predicting PATHOgen COMmunities

PATHOCOM

Corresponding Principal Investigator: Detlef Weigel
Host institution: Max-Planck-Gesellschaft zur Förderung der Wissenschaften

Other Principal Investigator: Fabrice Roux
Host institution: Centre National de la Recherche Scientifique

Other Principal Investigator: Joy Bergelson
Host institution: University of Chicago

Proposal duration: 72 months

Infectious disease is often the **major selective agent** in nature, and we cannot understand how populations evolve without understanding their **pathogenic microbes**. Beyond host immunity, an important factor determining the ability of pathogens to invade and proliferate in a host is the resident **microbiota**, but we are only beginning to glimpse its multifarious impacts. We know even less about interactions among pathogenic microbes themselves. Any effort to explain how **pathogen communities**, or pathobiota, develop within a host requires knowledge about the extent to which pathogens engage in competition, commensalism and cooperation, both with other pathogens and the rest of the microbiota. To date, studies of plant-pathogen interactions in the lab and descriptive work in the field have focused on **pairwise interactions** between one plant host and one pathogen, leaving a large gap in our understanding of how **different** types of interactions **between microbes**, and especially pathogens, determine the **outcome** of **host-pathogen interactions** in the **real world**. In PATHOCOM, we will implement a program that integrates large-scale **field observations** of microbes in *Arabidopsis thaliana* with **ultra-high-throughput experimental** tests of host-dependent interactions, allowing **experiment-informed modeling** of pathogenic microbe-microbe interac-

WRITING THE PROPOSAL: EXAMPLES FOR INSPIRATION

KNOWLEDGE GAP AND AIMS

Progress on multiple fronts notwithstanding, there are **important gaps** in our knowledge of plant-pathogen interactions, **especially** with **endemic pathogens**. We not only have limited insight into how molecules identified in the lab are deployed in natural conditions, but we also do not understand well how different types of interactions between pathogens determine the **outcomes** of **infection** in the **real world**. 16S rDNA and similar amplicon surveys of background microbiota have mostly led to the conclusion that "things are complicated". Here, we propose to fill these gaps in our understanding of real-world plant-pathogen interactions, in an ambitious program with the following **Specific Aims**:

1. Geographically **structured characterization** of *A. thaliana* and its complex **(patho)microbiota**
2. **Experimental** characterization of a spectrum of simplified pathogen-pathogen **interactions** *in planta*
3. Building a **model** of **persistent communities** from empirical pathogen-pathogen interactions
4. Experimental characterization of **(a)biotic factors modulating** pathogen-pathogen **interactions**
5. Applying the **model** in an **ecological genomics framework**

TANGIBLE SYNERGIES

PATHOCOM is not only of a scale that goes beyond the capability of an individual research group, but it also requires integration of a **team** that **combines diverse expertise** with **access** to **specialized facilities** and **well-understood field sites**. A key element is the effort to link diversity of important foliar microbes with diversity of their plant host and associated ecological variables in three distinct geographic regions, near each of the Principal Investigator's home institutions in France, Germany and the US. We have established **networks of natural sites** with ***A. thaliana*** **populations**, some of which we have followed for over 20 years. Through this foundational work, the three Principal Investigators have extensive experience with the behavior of *A. thaliana* in the field in different years and seasons. To obtain field data that are comparable between sites, all populations have to be closely monitored; to do this for several seasons would be infeasible at sites that are not within easy driving distance of the involved labs.

is beyond the capability of any single academic group. To ensure that data generated in a distributed fashion are directly comparable and thus **suitable** for **extensive mathematical modeling**, it is essential that **experimental methods** and **sampling strategies** are applied in an **identical manner** in the three groups, which can only be achieved by tight integration of experimental practices via multiple mutual, extended visits and secondments of students and postdocs over substantial periods of time.

source: Detlef Weigel, Fabrice Roux and Joy Bergelson, https://figshare.com/articles/preprint/PATHOCOM_proposal/13174337

SYNERGETIC WORKING ARRANGEMENTS

Ensuring team integration

The three Principal Investigators and their co-investigators already have a **proven record of collaboration**. To continue to ensure seamless integration of team members at the three sites, we will have (i) **monthly "all hands" meetings** by video conferencing at 9 am Chicago/4 pm European time, (ii) **weekly project meetings** by video conferencing, (iii) **joint field sampling efforts** (of note, Bergelson has carried out joint field experiments in Sweden for several years now with collaborators from Sweden, Austria and the UK), (iv) **mandatory secondments** of postdocs and PhD students, and (v) **annual multi-day retreats** rotating among the three sites. We will use two major tools for project management, information exchange and internal reporting. We will use **Slack** for rapid, informal communication between team members, and Atlassian's **Confluence** platform for long-term coordination. Confluence provides a powerful wiki-like platform for team collaboration, and it allows for secure sharing of data and information, reporting as well as assignment and tracking of experiments.

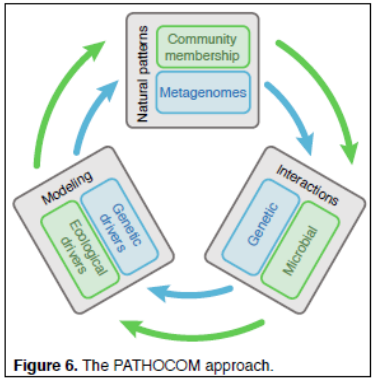


Figure 6. The PATHOCOM approach.

source: Detlef Weigel, Fabrice Roux and Joy Bergelson, https://figshare.com/articles/preprint/PATHOCOM_proposal/13174337

WORK OF THE GROUP LEADING UP TO THE PROPOSAL
PROOF OF PRINCIPLE-RESULTS/PRELIMINARY DATA

variation of disease resistance in both wild and cultivated plants[81]. Our team has **pioneered the successful application** of **GWA** studies in *A. thaliana* by (i) developing mapping populations at various geographical scales[31–33,38,45]; (ii) developing new statistical methods of GWA mapping including one for simultaneous GWA

We recently found that the **genetic architecture** of **disease resistance differs** when plants are **co-infected** with **multiple pathogens** instead of a single pathogen. In one specific case, the plant response to co-infection

For a proof of concept, we co-inoculated *A. thaliana* with two *P. viridiflava* strains expressing luciferase and 60 randomly chosen strains from the *P. syringae* complex (Fig. 1). Luciferase activity was measured after 36 hours to quantify abundance of the focal strains. Two key results reveal that **co-infection** strongly impacts pathogen performance in *A. thaliana*: (i) the

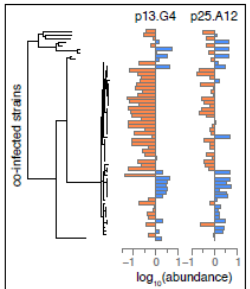


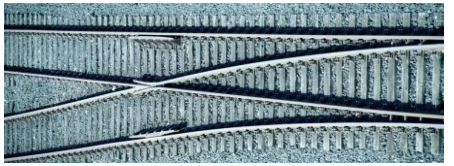
Figure 1. Pairwise co-infections of luciferase-tagged *P. viridiflava* strains isolated from *A. thaliana* and 60 other isolates whose phylogenetic relationship is shown on the left. Abundances of the focal strains in co-infections are expressed relative to single infections.

RISK-GAIN-BALANCE

How does PATHOCOM meet the high-risk/high-gain profile expected of ERC projects? PATHOCOM goes **beyond** the **current state of the art** by taking **full advantage** of very rapid developments in the **genomics** of **wild communities, ultra-high-throughput methods** for studying **microbe-microbe interactions** ***in planta*** and our ability to **model very large data sets**. With the exception of human gut microbiome research, we are not aware of other programs with similar ambitions to understand **drivers** of **microbe-microbe interactions** in the **real world**, at the **level** of **community, environment** and **genetics**. While lab studies have been very successful in informing us about general principles and mechanisms of pathogen recognition by the host, and evasion of recognition by pathogens, we are still largely in the dark when it comes to understanding how microbes interact in the **context** of **natural infections** to **overcome plant defenses**. We will redress this situation in PATHOCOM.

Our aims span a **range** of **approaches** with **increasing risk**. Aim 1 will deliver **rich knowledge** about

CONTINGENCY PLANNING

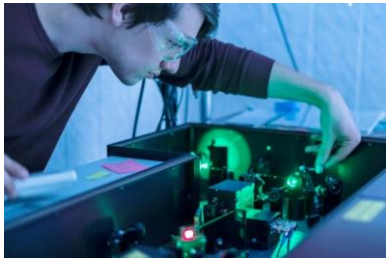


Contingency planning: The proposed methods are already in place, and we have long experience with the field sites that we will sample. The greatest risk is that individual A. thaliana *populations disappear or sites are destroyed by development, but in each of the regions, we can easily choose from additional sites. We estimate that over the course of three years, fewer than 4 of the 20 sites in each region are at risk. A final risk is that our PEN-seq enrichment baits do not include all causal genes, but core genome relatedness should still capture at least in part patterns of sharing of causal non-core genome genes, plus we can resort to the WGS data for additional gene discovery (although these will be relatively low coverage).*

Contingency planning: One risk is that the direct integration of barcodes into plant genomes might turn out to be too inefficient. In this case, we will adopt the GESTALT method for generating barcodes in a special transgene[130]. Regarding GWA mapping, the effect of population structure is always highly dependent on the trait considered[38]. If population structure leads to an inflation of false negatives[30,131], we will reduce population structure by performing GWA mapping separately within each region (France, Germany, USA). The genetic architecture underlying natural variation of microbe-microbe interactions can be unpredictable as well. If allelic effects of candidate genes are marginal[132], we will create lines that contain multiple mutations/overexpress multiple genes.

Feasibility; favourable risk-gain-balance:
Plan B/mitigation strategies; access to instruments, beam time, archives,....

FOCUS/PRIORITIES EXPLAINED



pected to be pathogenic). Fungi and oomycetes can be found within the microbiota of *A. thaliana*[43,54–56], but we have chosen here to focus on **bacteria** due to (i) their dominance in *A. thaliana* microbiota by number and biomass[56,57], (ii) disease symptoms in natural populations of *A. thaliana* mainly resulting from pathogenic bacteria[25], and (iii) their **genetic tractability**, which will be essential for our ultra-high-throughput infection tests. We will, however, obtain information on eukaryotic microbes in our field sampling and can include such information in our models

ambitious scope ⟷ well-justified focus

convincing justification for your choices/priorities within the project

VALIDATION OF RESULTS

To **confirm** the causal role of **candidate genes** identified by joint GWA mapping, we will functionally validate up to 50 candidates using classical molecular genetics (e.g., marker-exchange deletion, complementation by chromosomal insertion etc.). Candidates will be chosen according to criteria such as type of interactions (with a preference for positive interactions), intra- vs. interspecific interactions (with a preference for pathogen-pathogen interactions), and percentage of variance explained by GWA hits. These efforts will directly allow for estimating false positives in the GWA analyses.

Can the results be generalised?

significance, explanatory power of results

CHARTS, FIGURES TO ILLUSTRATE OR DOCUMENT

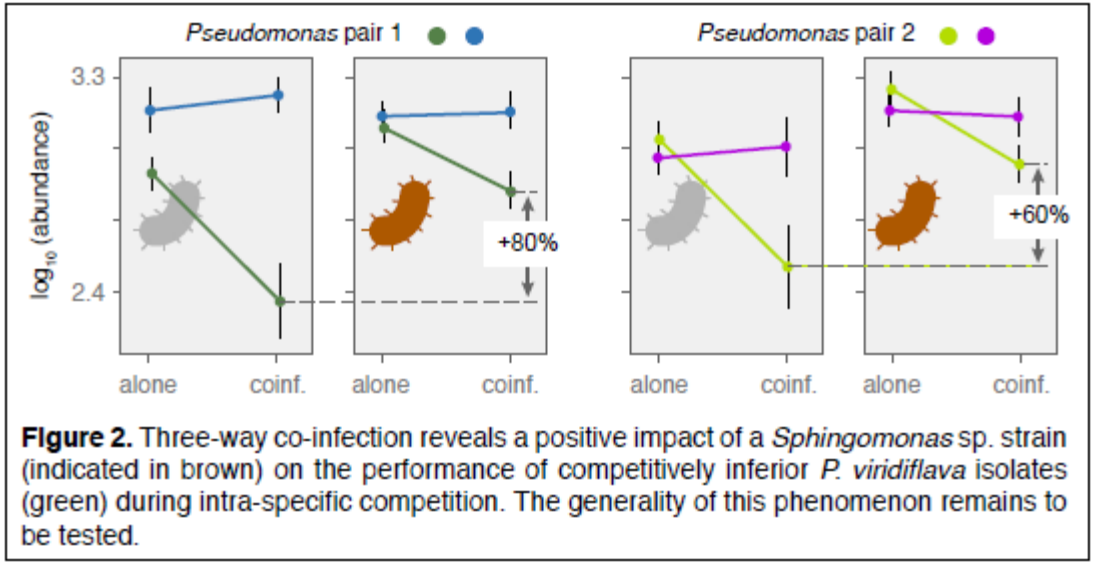


Figure 2. Three-way co-infection reveals a positive impact of a *Sphingomonas* sp. strain (indicated in brown) on the performance of competitively inferior *P. viridiflava* isolates (green) during intra-specific competition. The generality of this phenomenon remains to be tested.

source: Detlef Weigel, Fabrice Roux and Joy Bergelson, https://figshare.com/articles/preprint/PATHOCOM_proposal/13174337

feedback-loops with specialists and generalists

USEFUL LINKS & FURTHER INFORMATION

- ERC homepage: https://erc.europa.eu/
- ERC evaluation panels: https://erc.europa.eu/document-category/evaluation-panels
- ERC funded projects database: https://erc.europa.eu/projects-figures/erc-funded-projects
- Funded ERC Proposals published online: FFG collection at https://www.ffg.at/europa/heu/erc/published-proposals
- For a **proposal check by FFG** (focusing on structural features): Please send your proposal to erc@ffg.at by **mid-October**, 2023

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