Mechano-Wolbachia

Uncovering the mechanisms of action of an antiviral bacterium

Ewa Chrostek
Jagiellonian University
I have a vision of how to transform Wolbachia research
Wolbachia

Intracellular bacterium

O’Neill et al., PLoS Biol 2004
Wolbachia
Intracellular bacterium
Wolbachia protects flies from viruses

Drosophila C virus infection

**Wolbachia** protects flies from viruses

*Drosophila* C virus infection

Wolbachia protects mosquitoes from viruses

Dengue virus RNA copies

Moreira et al., 2009. Cell
Wolbachia-infected mosquito releases to fight dengue
Wolbachia-infected mosquito releases to fight dengue

Indonesia:
• 77% reduction in infections
• 86% reduction in hospitalization
What is the mechanism of *Wolbachia*-conferred antiviral protection?
What is the mechanism of *Wolbachia*-conferred antiviral protection?

None of the known antiviral mechanisms...
ERC StG Mechano-Wolbachia

Obj. 1. Establish model system.

Obj. 1.1. Determine when and where protection starts. Discover which genes are involved.

Obj. 1.2. Validate cell culture model.

Obj. 2. Discover molecular bases of antiviral protection.

Obj. 2.1. Use novel tools to pinpoint genes causing protection.

Obj. 2.2. Develop new tools.
1.1. Determine when and where protection starts

State-of-the art

Whole organisms

Late timepoints
1.1. Determine when and where protection starts

State-of-the art
- Whole organisms
  - Late timepoints

Mechano-Wolbachia
- Tissues
  - Early timepoints
1.1. Discover which genes are involved

State-of-the art

Whole organisms

Late timepoints

Mechano-Wolbachia

Tissues

Early timepoints

Genes involved in protection
Obj. 1. Establish model system.

Obj. 1.1. Determine when and where protection starts. Discover which genes are involved.

Obj. 1.2. Validate cell culture model.

Obj. 2. Discover molecular bases of antiviral protection.

Obj. 2.1. Use novel tools to pinpoint genes causing protection.

Obj. 2.2. Develop new tools.
2. Molecular bases of protection unknown.
2. Molecular bases of protection unknown.

Previously, no tools to study Wolbachia gene functions directly.
2. Molecular bases of protection unknown.

Previously, no tools to study *Wolbachia* gene functions directly.

I developed tools to do it!
Long-term gains

Scientific:

• Discover mechanisms of *Wolbachia* phenotypes
• Develop tools to study other unculturable microbes
• Use *Wolbachia* as a vector in insects
Long-term gains

**Scientific:**
- Discover mechanisms of *Wolbachia* phenotypes
- Develop tools to study other unculturable microbes
- Use *Wolbachia* as a vector in insects

**Societal:**
- Improve vector control efforts
- Preserve health of beneficial insects
- Use beyond *Wolbachia* or insects...
Who was I?

4+1 year

Gulbenkian Institute

FCT PhD Fellowship

First genotype-phenotype link in unculturable *Wolbachia*
Who was I?

4+1 year

Gulbenkian Institute
FCT PhD Fellowship

First genotype-phenotype link in unculturable Wolbachia

2 years

Max Plank Institute for Infection Biology
EMBO Long Term Fellowship

Standards for reporting of infection with unculturable bacteria
Who was I?

4+1 year
Gulbenkian Institute
FCT PhD Fellowship

2 years
Max Plank Institute for Infection Biology
EMBO Long Term Fellowship

4 years
University of Liverpool
FEBS Long Term Fellowship
Marie Skłodowska-Curie IF

First genotype-phenotype link in unculturable *Wolbachia*

Standards for reporting of infection with unculturable bacteria

Tools to study *Wolbachia* gene function!!!
Who was I?

- **Gulbenkian Institute**
  - 4+1 year
  - FCT PhD Fellowship

- **Max Plank Institute for Infection Biology**
  - 2 years
  - EMBO Long Term Fellowship

- **University of Liverpool**
  - 4 years
  - FEBS Long Term Fellowship
  - Marie Skłodowska-Curie IF

- **4 individual fellowships**
- **10 first-author publications**
- **8 invited talks**
- **7 awards for professional achievements**
Who was I?

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FCT PhD Fellowship

Max Plank Institute for Infection Biology
EMBO Long Term Fellowship

University of Liverpool
FEBS Long Term Fellowship
Marie Skłodowska-Curie IF

I was first told to apply for an ERC StG on the day of my PhD Thesis defence!
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Who was I?

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2 years
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I applied here
What did I do for those 6 years?

https://erc.europa.eu/apply-grant/starting-grant
Who can apply?

Researchers of any nationality with 2-7 years of experience since completion of PhD, a scientific track record showing great promise and an excellent research proposal can apply.

https://erc.europa.eu/apply-grant/starting-grant
ERC is a grant for the best scientists:

• Students of the best

• Collaborators of the best

• Mentees of the best
Get an idea

Combination of:

- Absolutely safe (but laborious and tedious) work no one has thought of doing before,

- Innovative/groundbreaking experiments.
What has helped me get the grant?
What has helped me get the grant?

National Contact Point and the lessons learned
What has helped me get the grant?

National Contact Point and the lessons learned
What has helped me get the grant?

National Contact Point and the lessons learned

CV & track record should tell a story

Stress on independence

International outlook
What has helped me get the grant?

National Contact Point and the lessons learned

CV & track record should tell a story

Stress on independence

International outlook

Write to generalists

Stress impact (if successful)

Ask as many people as possible to read/provide feedback
What has helped me get the grant?

National Contact Point and the lessons learned

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<tr>
<td>CV &amp; track record should tell a story</td>
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<tr>
<td>International outlook</td>
<td>Ask as many people as possible to read/provide feedback</td>
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<td>Write to people in your field – you’ve got this!</td>
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What has helped me get the grant?

National Contact Point and the lessons learned

Interview

Think about it as a “ted talk”

Practice!

Questions: 3 sentences and stop talking
Who has helped me get the grant?

Mentors and people who care

Seek people who are “good at getting grants”

Help others so that you get help when needed

Network, network, network!

Ask, ask, ask!
What has helped me get the grant?

The best science is brave; it breaks the convention and investigates new realms.

Proposal must be innovative BUT you have to prove it is feasible.
What has helped me get the grant?

Choose your panels wisely

PHYSICAL SCIENCES AND ENGINEERING (PE)
LIFE SCIENCES (LS)
SOCIAL SCIENCES AND HUMANITIES (SH)
What has helped me get the grant?

Choose your panels wisely

LIFE SCIENCES (LS)

Integrative Biology: From Genes and Genomes to Systems (LS2)

Immunity, Infection and Immunotherapy (LS6)

Prevention, Diagnosis and Treatment of Human Diseases (LS7)

Environmental Biology, Ecology and Evolution (LS8)
What has helped me get the grant?

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What has helped me get the grant?

Do not underestimate your CV

No Nature, Science, Cell papers

Stress on international outlook

Stress every achievement
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Thank you for your attention & good luck with your proposals!