Functional Investigation of PE_PGRS Proteins and Their Role in Mycobacterial Virulence

Liz White

About Me

- Cleveland, Ohio and Pittsburgh, Pennsylvania
- Colorado College
- Molecular Biology
- Research Background
  - Conducted Gateway cloning experiments to investigate how the gene MBL-1 acts as a splicing factor required for dendrite patterning in C. elegans
- Plan to pursue a Phd and continue in the medical research field
- art, running, dance, travel

COLORADO COLLEGE

Project Background

Mycobacteria

- Mycobacterium tuberculosis is the leading cause of infectious disease-related deaths worldwide
- Nontuberculous mycobacteria (NTM) infections are increasing
  - Form biofilms on household and hospital surfaces
  - resistant to many commonly used antibiotics
  - Immunocompromised individuals and the elderly are at highest risk
- mechanisms of virulence and pathogenesis are not yet fully understood

Saxena, S., Spaink, H. P., & Forn-Cuní, G. (2021). Drug Resistance in Nontuberculous Mycobacteria: Mechanisms and Models. Biology, 10(2), 96. https://doi.org/10.3390/biology10020096

PE_ PGRS Protein Family

- virulent mycobacteria
- on the bacteria's surface or excreted
- promote mycobacterial survival:
  - mediating bacterial entry
  - modulating host anti-mycobacterial inflammatory responses
  - lipid metabolism
  - cell death

Sharma, T., Alam, A., Ehtram, A., Rani, A., Grover, S., Ehtesham, N. Z., & Hasnain, S. E. (2022). The Mycobacterium tuberculosis PE_PGRS Protein Family Acts as an Immunological Decoy to Subvert Host Immune Response. International journal of molecular sciences, 23(1), 525. https://doi.org/10.3390/ijms23010525

Research Focus

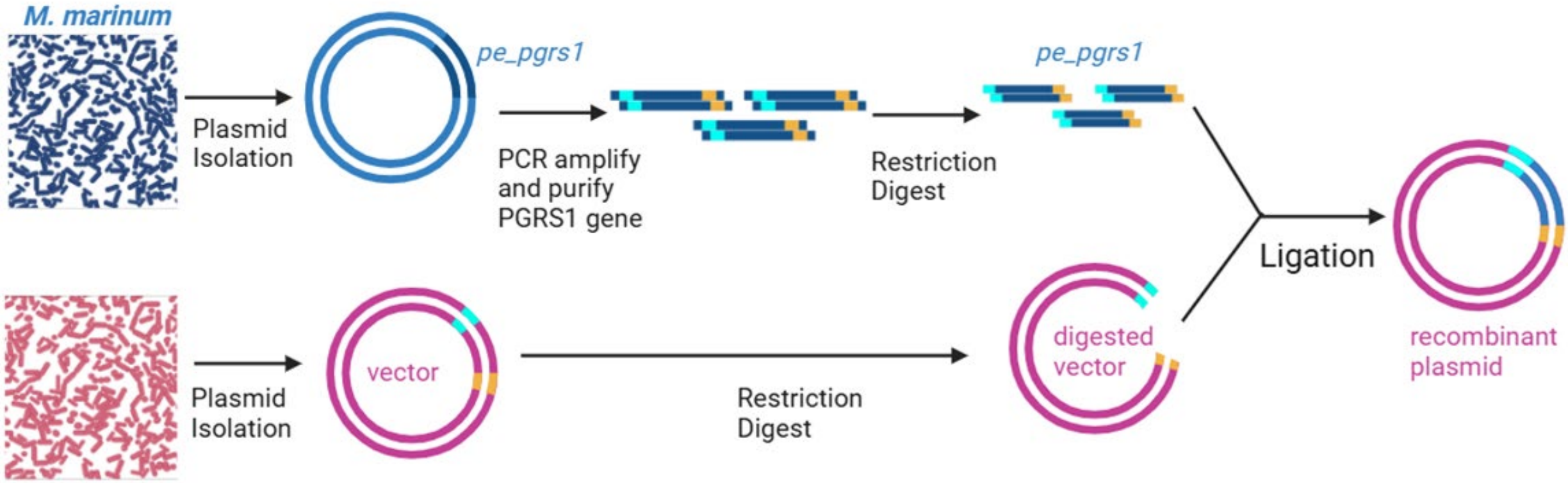
- What role does PE_PGRS1 play in mycobacterial virulence?

- To address this, we will:
  - Express the PE_PGRS1 protein from *M. marinum* (pathogenic species) in *M. smegmatis* (non-pathogenic species)
  - Investigate its effects using a zebrafish infection model

pe_pgrs1

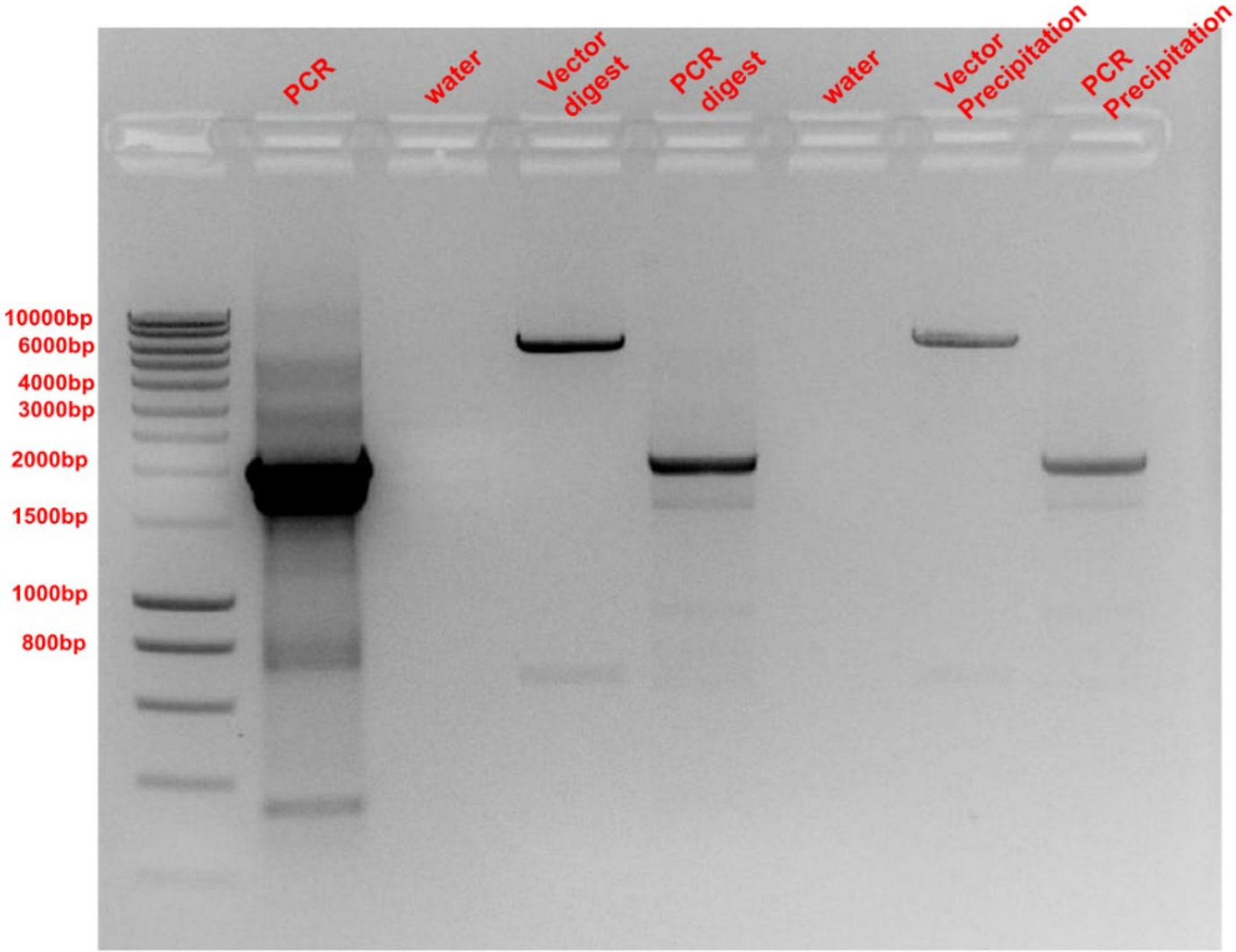
PE_PGRS protein

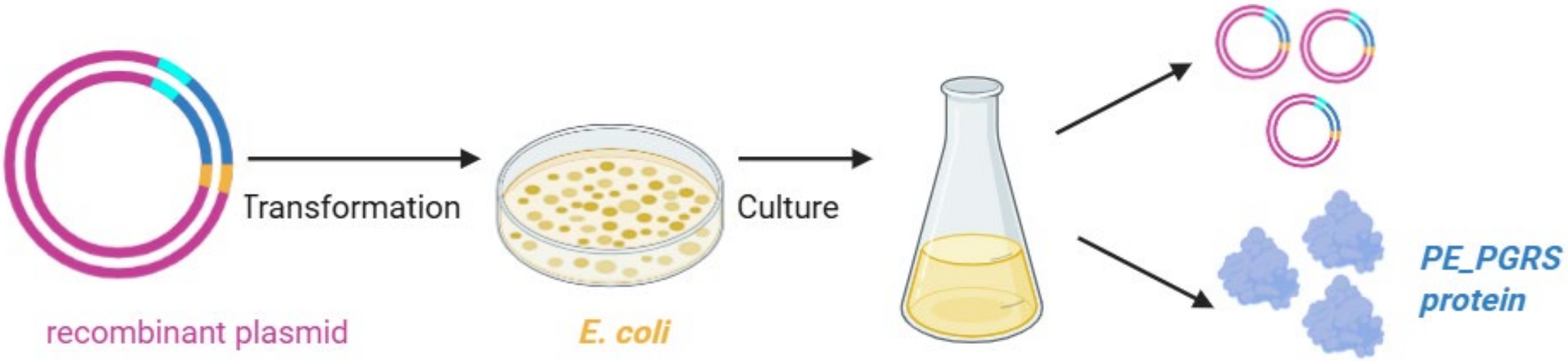
Current Progress


M. marinum
Plasmid Isolation
pe_pgrs1
PCR amplify and purify PGRS1 gene
pe_pgrs1
Restriction Digest
Plasmid Isolation
vector
Restriction Digest
digested vector
Ligation
recombinant plasmid

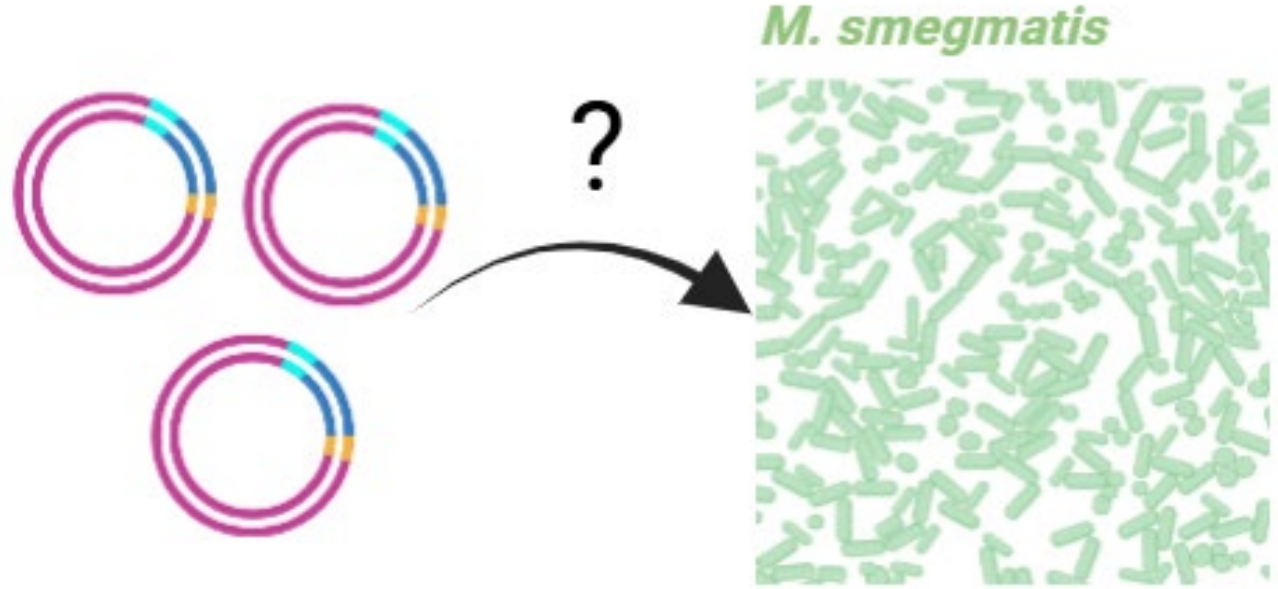
Gel Electrophoresis of

- PCR-amplified *pe_pgrs*1 gene
- Restriction Digest
- DNA Precipitation




Transformation
Culture
recombinant plasmid
E. coli
PE_PGRS
protein

Current Questions



- How will PE_PGRS1 affect the virulence of *M. smegmatis*?

- How does the overexpression of PE_PGRS1 in *M. smegmatis* affect the inflammatory response in zebrafish larvae?

Importance

PE_PGRS proteins could be targets for TB and NTM diagnosis, as well as drug and vaccine development

pe_pgrs1

PE_PGRS protein

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European Undergraduate Research Opportunities

Thank You!

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