



Grand Challenges
African Drug Discovery
Accelerator

Convening Meeting 2025

TB Flagship Project Presentation

Erick Strauss

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GC ADDA4TB Team



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PI: Erick Strauss

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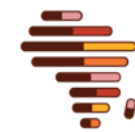
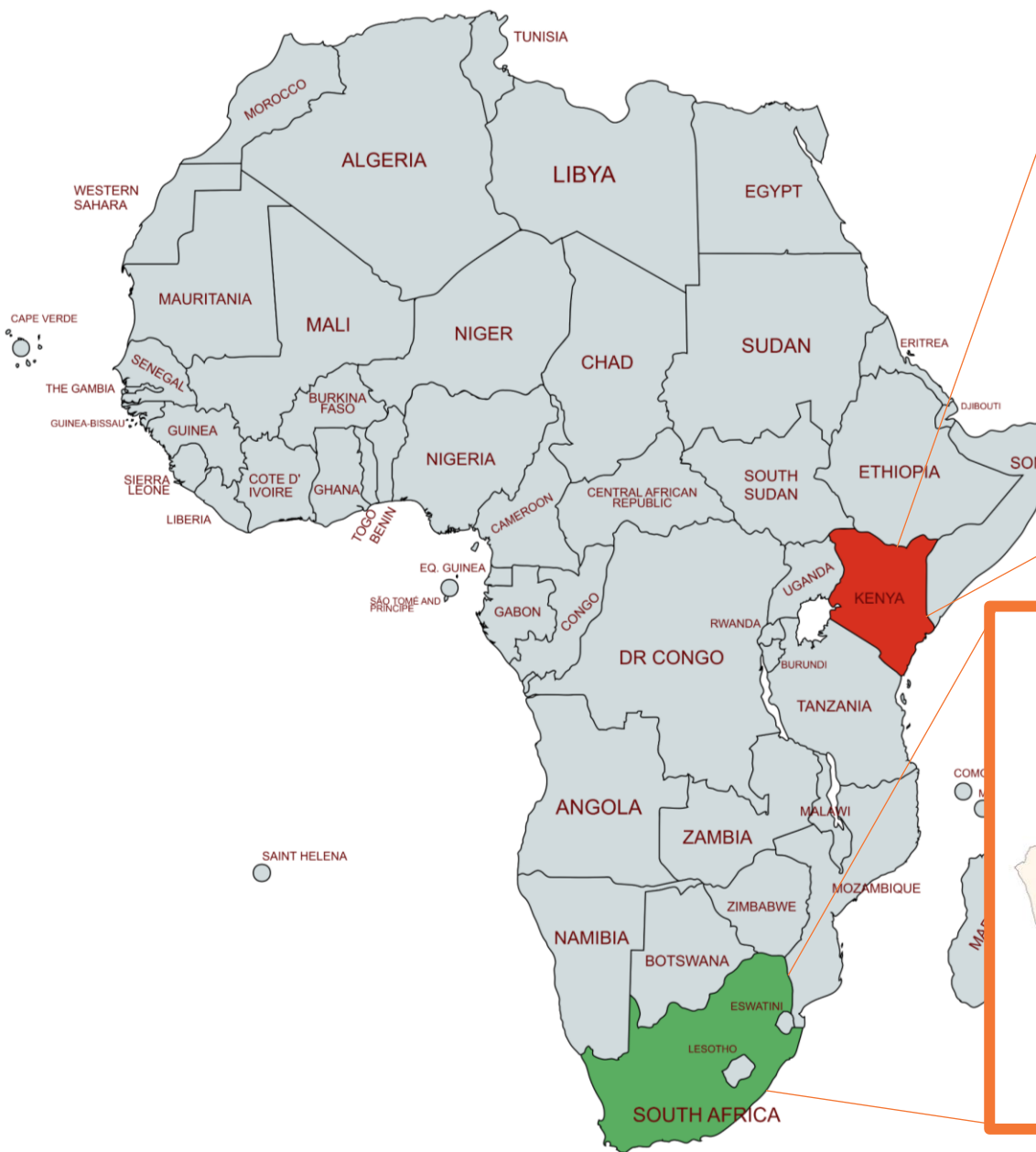
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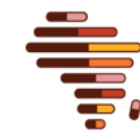


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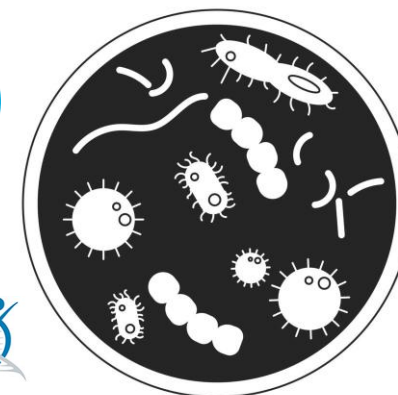
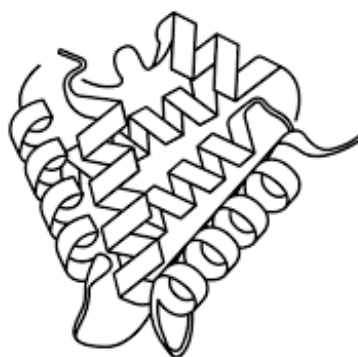
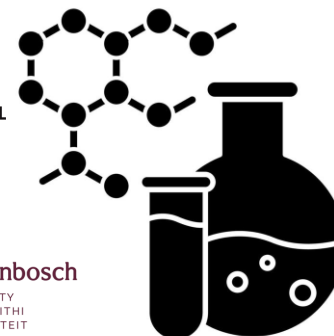
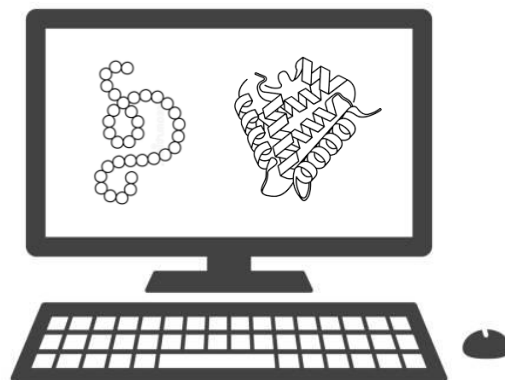


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Where leaders learn

GC ADDA4TB - Expertise



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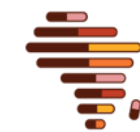




GC ADDA4TB - Vision

Pursuing Targeted Protein Degradation for Anti-TB Drug Development

GC ADDA4TB - Background

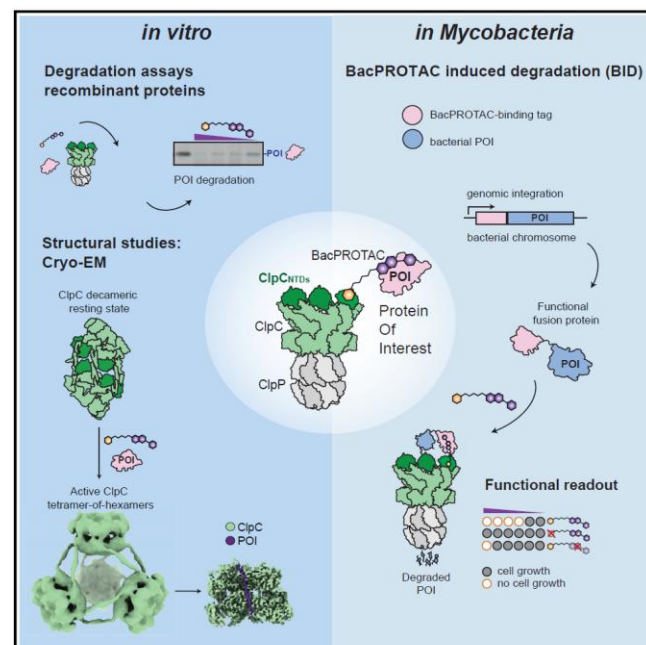


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Cell

BacPROTACs mediate targeted protein degradation in bacteria

Graphical abstract



Morreale, Francesca E., et al. "BacPROTACs mediate targeted protein degradation in bacteria." *Cell* 185.13 (2022)

Authors

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In brief

Small-molecule adaptors, BacPROTACs, redirect bacterial ClpCP protease to target neo-substrates in a highly specific manner and expand targeted protein degradation technology to bacteria.

nature communications



Article

<https://doi.org/10.1038/s41467-024-46218-7>

Homo-BacPROTAC-induced degradation of ClpC1 as a strategy against drug-resistant mycobacteria

Received: 28 October 2022

Accepted: 12 February 2024

Published online: 05 March 2024

Check for updates

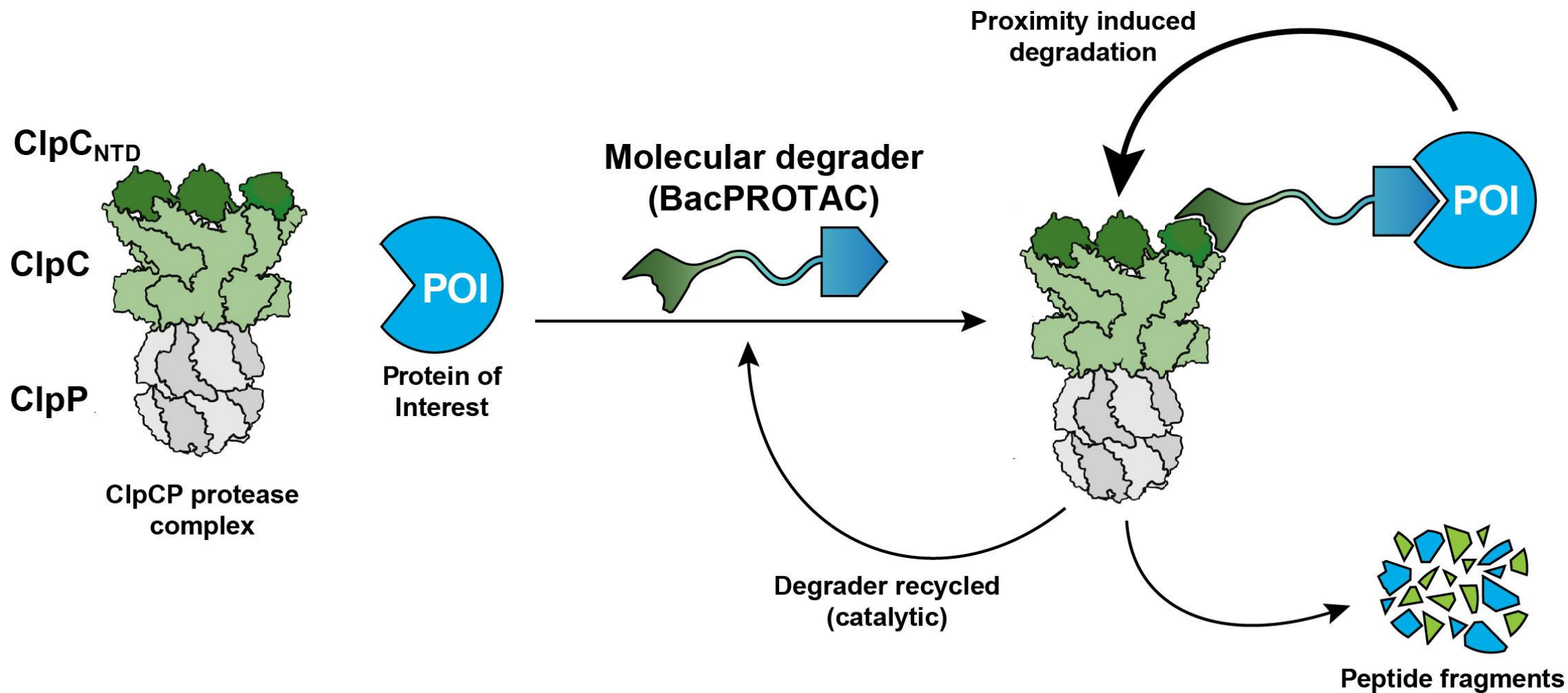
Lukas Junk^{1,6}✉, Volker M. Schmiedel^{2,6}, Somraj Guha¹, Katharina Fischel², Peter Greb², Kristin Vill³, Violetta Krisilia³, Lasse van Geelen³, Klaus Rumpel², Parvinder Kaur⁴, Ramya V. Krishnamurthy⁴, Shridhar Narayanan⁴, Radha Krishan Shandil⁴, Mayas Singh⁴, Christiane Kofink², Andreas Mantoulidis², Philipp Biber², Gerhard Gmaschitz², Uli Kazmaier¹, Anton Meinhart⁵, Julia Leodolter⁵, David Hoi⁵, Sabryna Junker⁵, Francesca Ester Morreale⁵, Tim Clausen⁵, Rainer Kalscheuer³, Harald Weinstabl²✉ & Guido Boehmelt²✉

Junk, Lukas, et al. "Homo-BacPROTAC-induced degradation of ClpC1 as a strategy against drug-resistant mycobacteria." *Nature Communications* 15.1 (2024)

GC ADDA4TB - Mission



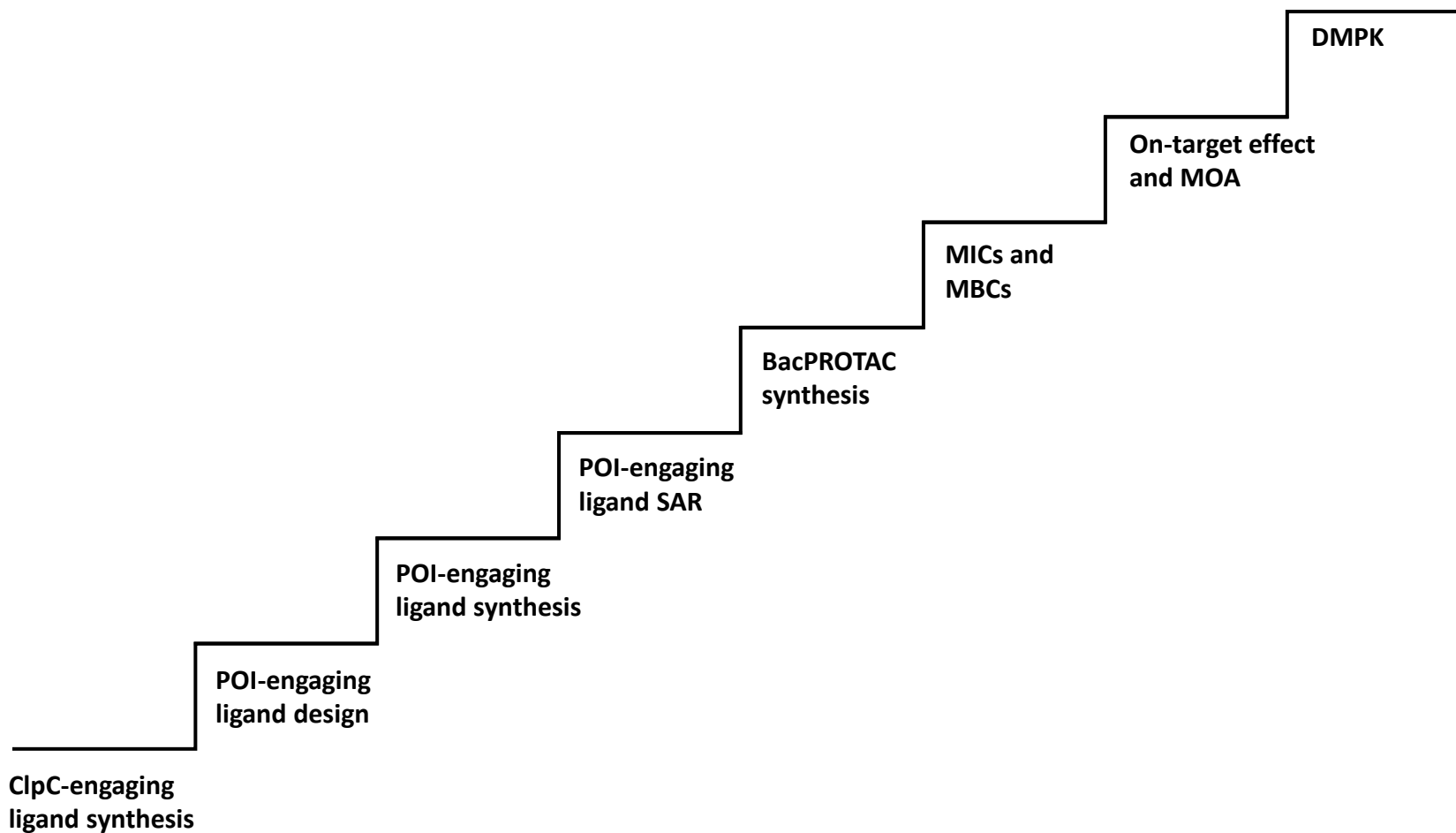
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GC ADDA4TB – Starting point



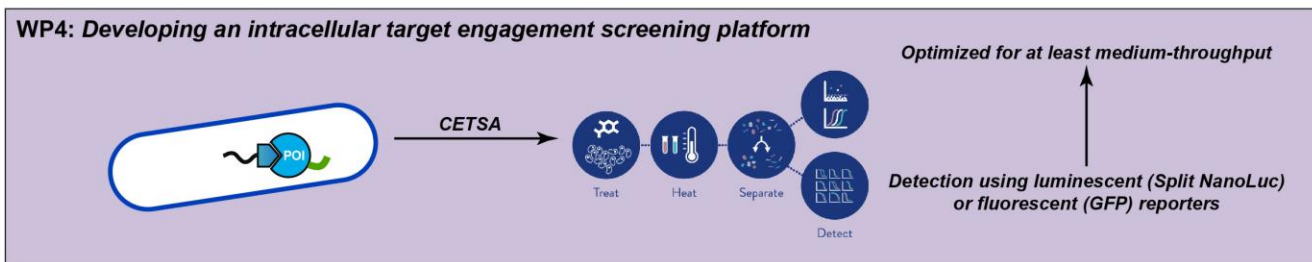
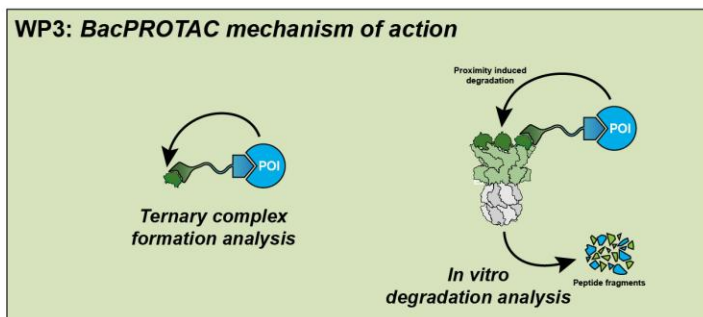
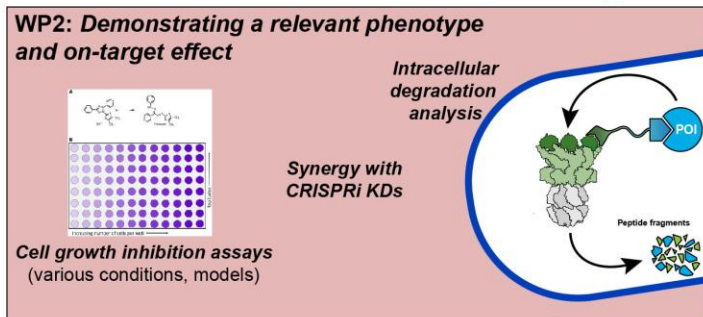
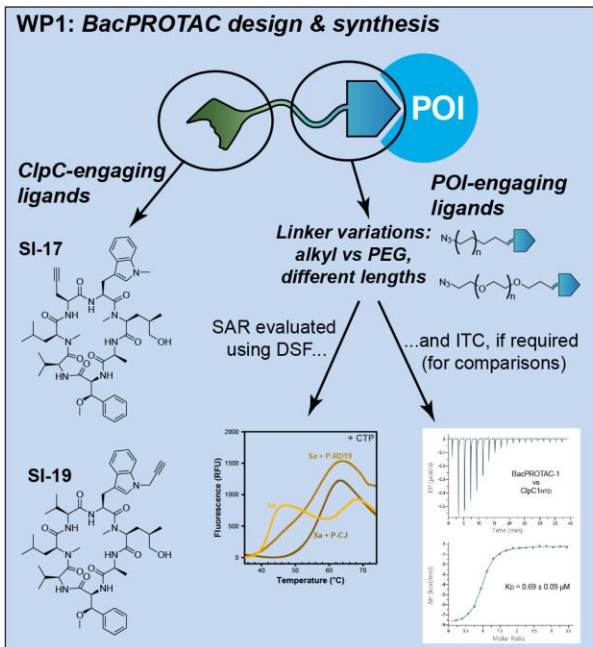
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GC ADDA4TB - Approach

Time



Develop generic workflow



Proof of concept targets



Establish generic workflow

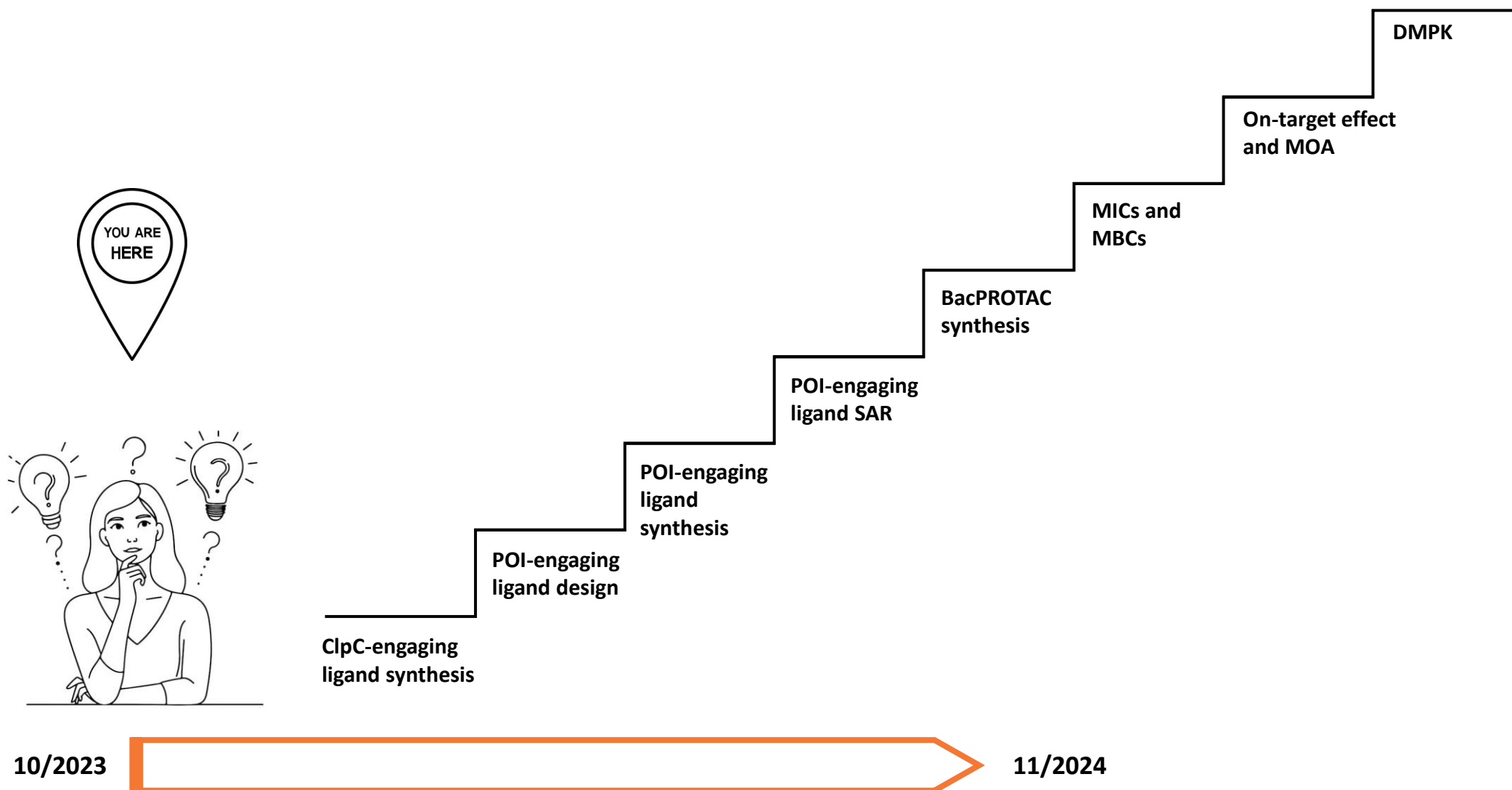


High value targets

GC ADDA4TB – Progress



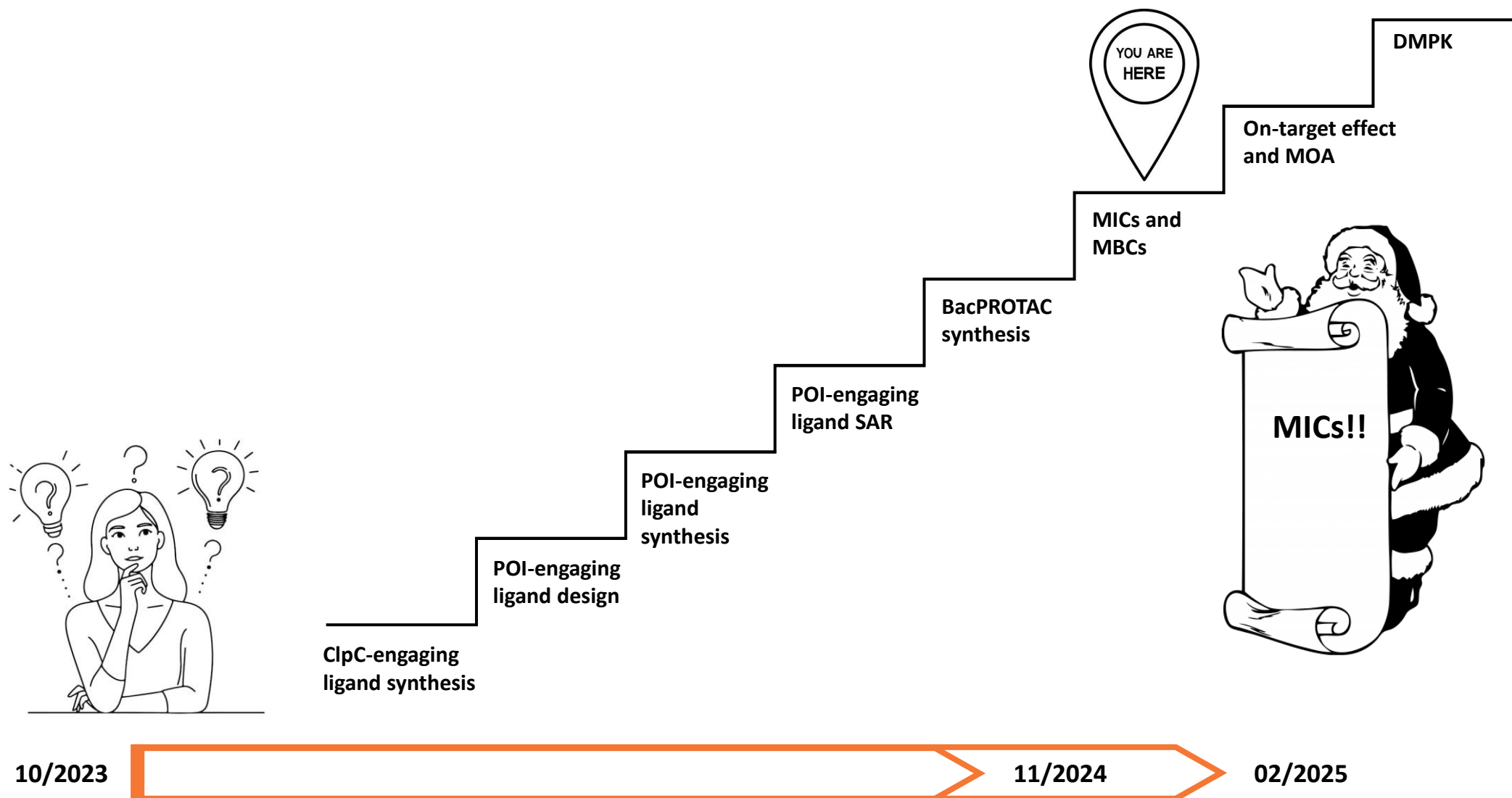
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GC ADDA4TB – Progress

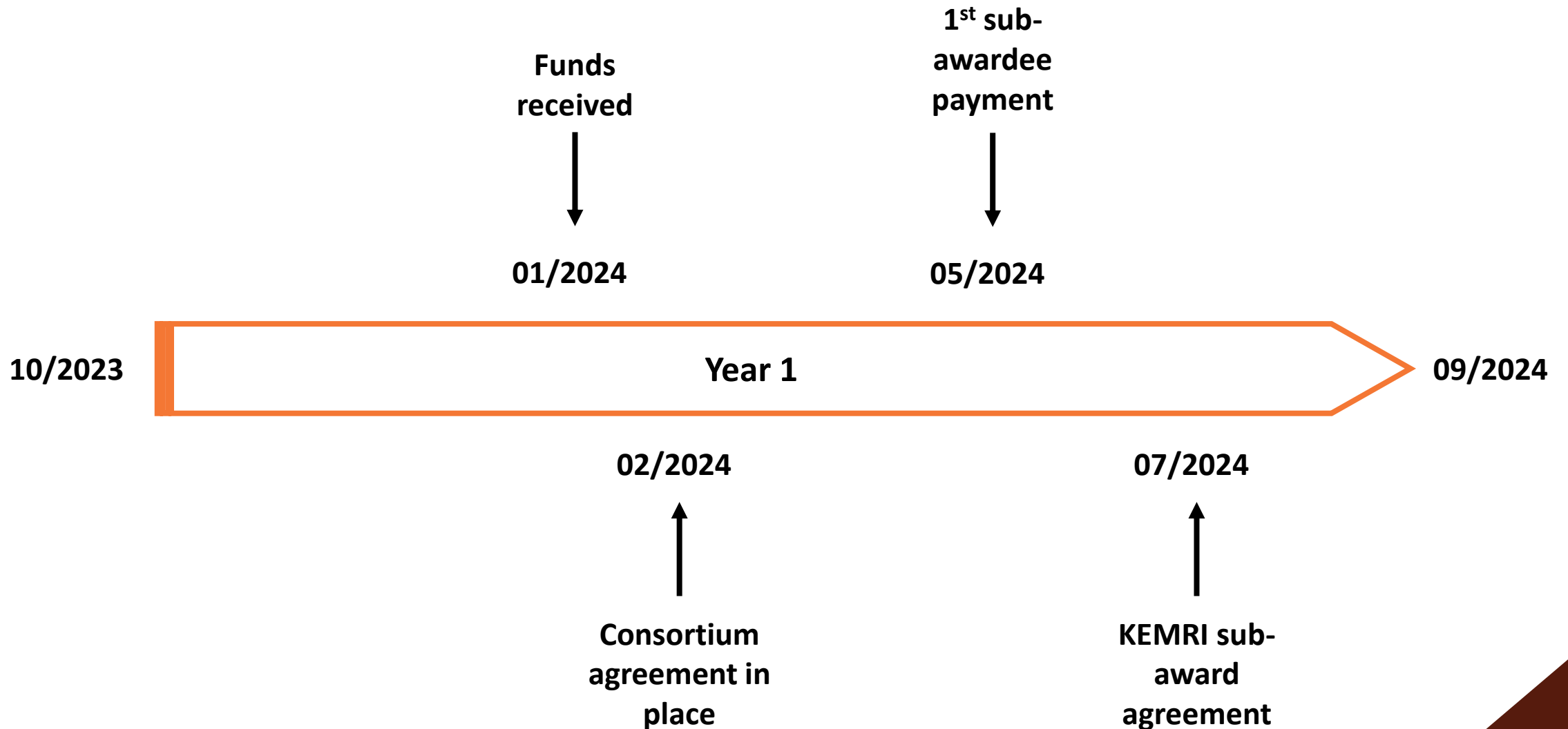


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Project Initiation Challenges





Project Initiation Challenges



- Working with institutional legal teams from the start is crucial
- Getting timely approval from institutional research heads can be slow
- Advanced notices and regular follow-ups and building relationships with these offices help



Project Initiation Challenges



- **Accountants and systems** that do not have a lot of experience with implementing specific project requirements (e.g. 50/50 split of expenses)
- PI input and engagement with institutional offices/leaders is crucial
- Dedicated institutional research project accountants or training platforms would be very useful
- Don't be the first to start a project on a new grant management system 😊

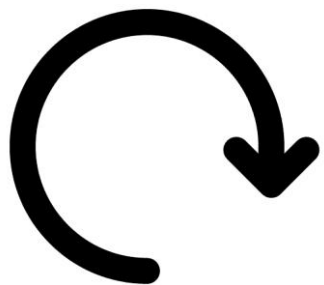


Project Initiation Challenges



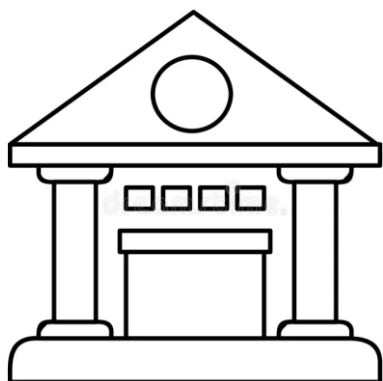
- **Personnel recruitment** on a short time frame is challenging
- Most of the sites have small groups (4-7 students)
- Pivoting PhD projects and postdocs funded by other grants not always possible, but these continue
- Recruiting postdocs from abroad is challenging
- Recruiting within your own student group or institution (or established network) is sometimes the best/only option to ensure progress

Project Initiation Considerations



- **Project initiation dates** should be negotiated as far as possible
- Have **3 month setup period** before kick-off to allow:
 - getting institutional project infrastructure in place
 - Consortium and sub-award agreements in place
 - Recruit and get students and postdocs in place
- **No-cost extensions** should be negotiated early as an alternative

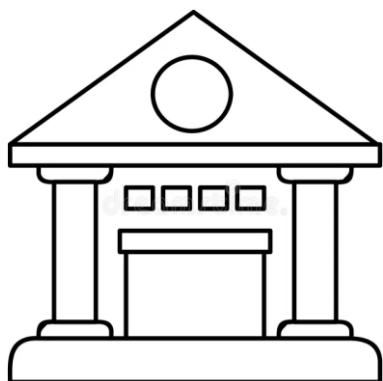
Institutional Challenges



- Each institution has its own challenges and strengths from an administrative perspective – good to **be aware of these** in advance
- **International payment** challenges:
 - Requires specific permission from the SA Reserve Bank (exchange control application)
 - 4-8 weeks. Has to be renewed every 12 months



Institutional Challenges



- **Government organisations** pose specific challenges, e.g. requirement of government tendering procedure for procurement of goods and instruments
- **Alternatives** for such organisations:
 - Limit payments to salaries
 - Use third party agents for other purchases and payments
 - Need appropriate contracts/agreements to be negotiated and set in place

Key lessons learned: Shipping



- Working with a **courier** company that has a good relationship with your institution can be very beneficial
- Quick **customs clearance** is made possible by billing institutional account without requiring immediate payments
- Having actual **contact persons** at the company is very helpful



Key lessons learned: Comms



- **Open communication platform** (e.g. Slack)
 - very useful to ensure timely, directed communication
 - promotes collaboration and keeps everyone in the loop
 - **but** requires stakeholder buy-in
- **Project meetings**
 - important to maintain a regular schedule
 - crucial to involve the entire team (including postdocs, PhD students) for closed communication loop



Key lessons learned: PM



- Use of **project management tools** to
 - keep track of objectives and progress
 - align activities to reporting requirements
 - assist with budget planning and reassignment



Key lessons learned: CROs



- Project required rapid access to complex (known) chemical entity – not possible within project team
- Lack of CROs for chemical synthesis on continent lead to engagement of Chinese CRO
- Developing relationships with CRO team and managers is key – building trust
- Engagement of CROs still require competency in the Africa-based teams to evaluate/direct project progress
- African team became crucial to project success



Key lessons learned: Chemical procurement



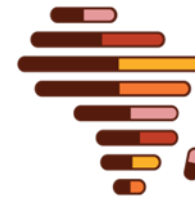
- Access to chemicals/reagent with **shipping restrictions** is severely limited
- **Delayed orders** from usually trustworthy local suppliers (6-12+ months)
- **Cause of delays**/expected ETAs not clearly communicated
- **Alternative** international **suppliers** exist, but each shipment attracts international shipping fees
- Logistics company for network activities/needs?



Successes



- Establishing a **functioning team** of previously unrelated members in a short timeframe
 - Building relationships and trust
 - Access to new expertise and wider network of connections
- **From zero to hero** (1st MICs!) in <12 months
- **CDD Vault access**
 - crucial for a drug discovery projects
 - training and support readily available
 - appointing CDD champions at each site
- **Project manager:** skills development & growth



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Thank you!

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