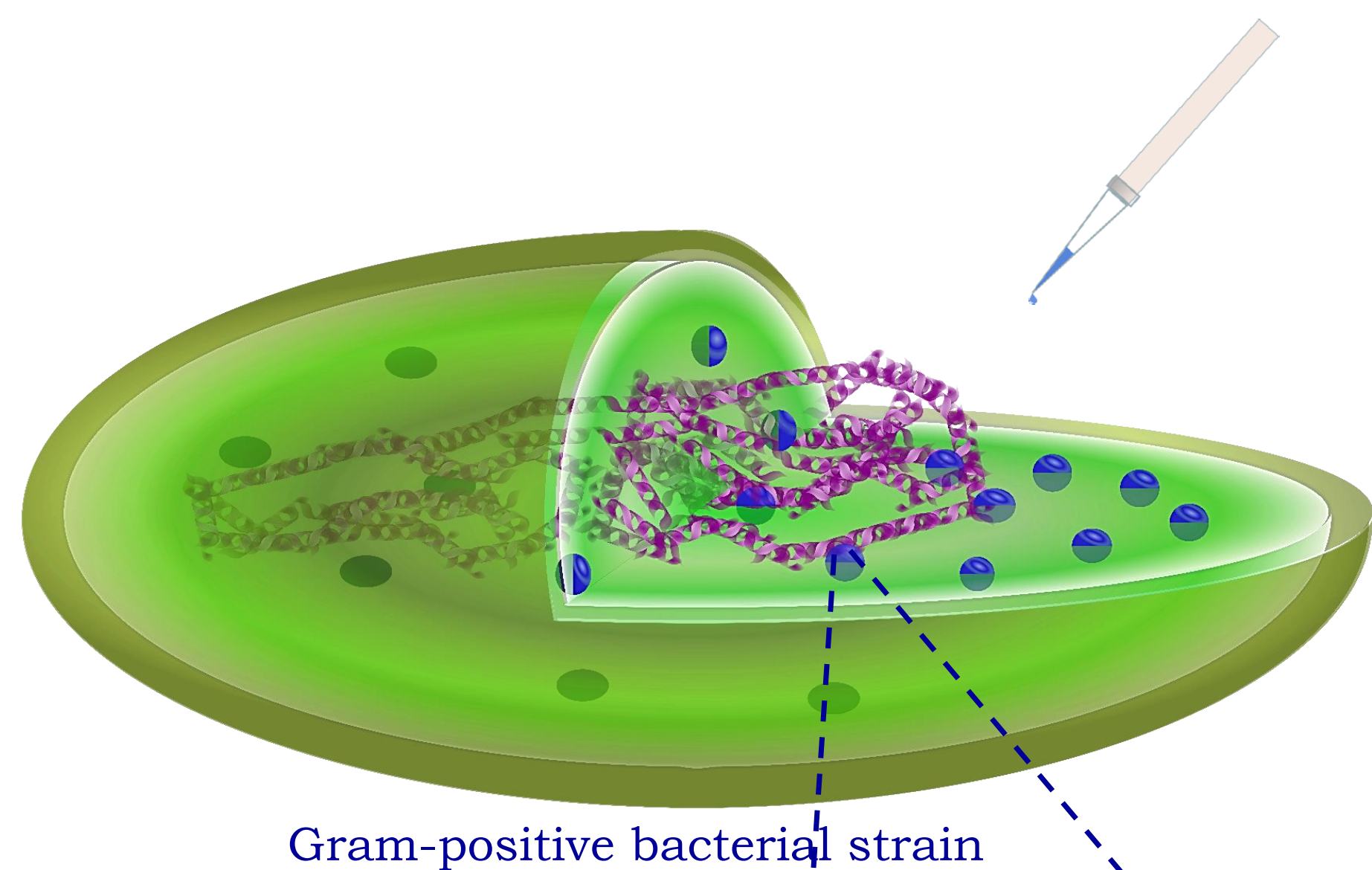


Radica Arnaudova¹, Cristina Durante Cruz², Alexandros Kiriazis¹, Ingo Aumüller¹, Jari Yli-Kauhaluoma¹, Päivi Tammela²

¹Drug Research Program, Division of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy, P.O. Box 56, FI-00014 University of Helsinki, Finland

²Drug Research Program, Division of Pharmaceutical Biosciences, Faculty of Pharmacy, P.O. Box 56, FI-00014, University of Helsinki, Finland



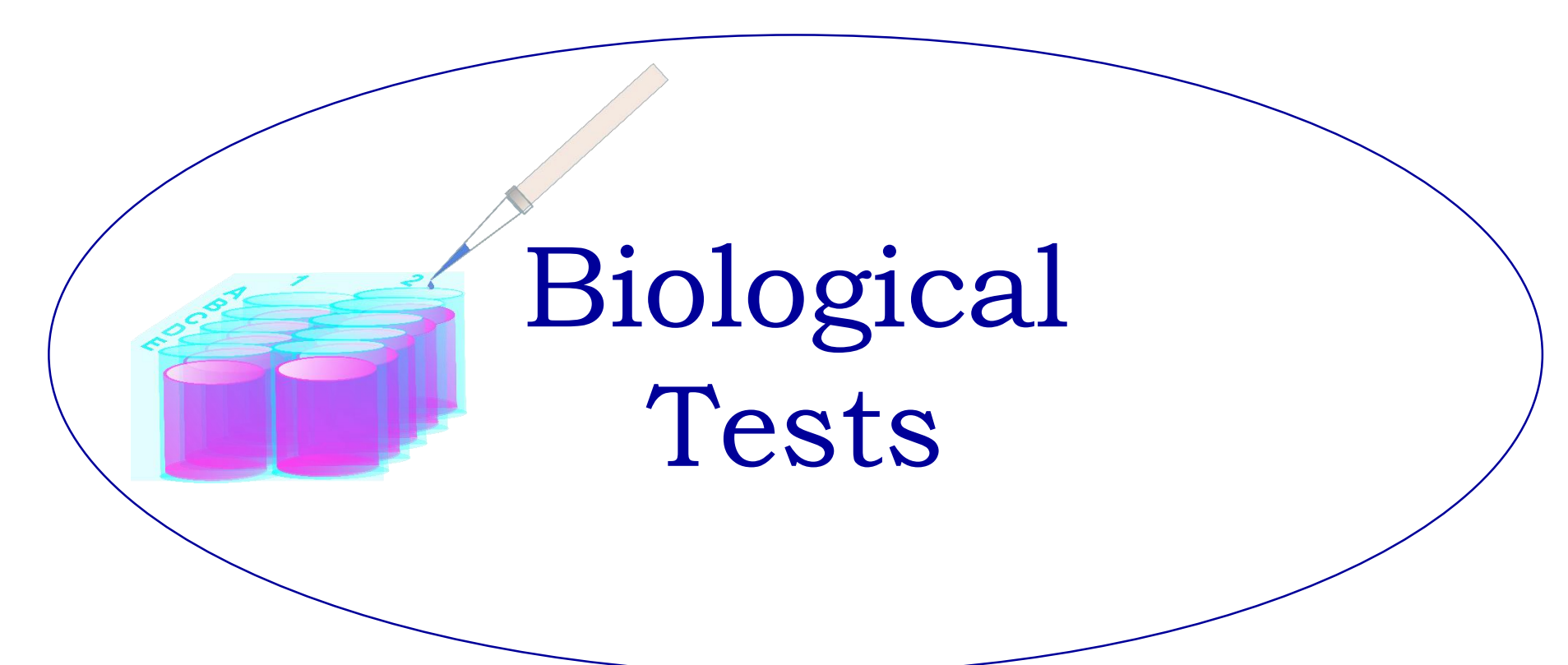
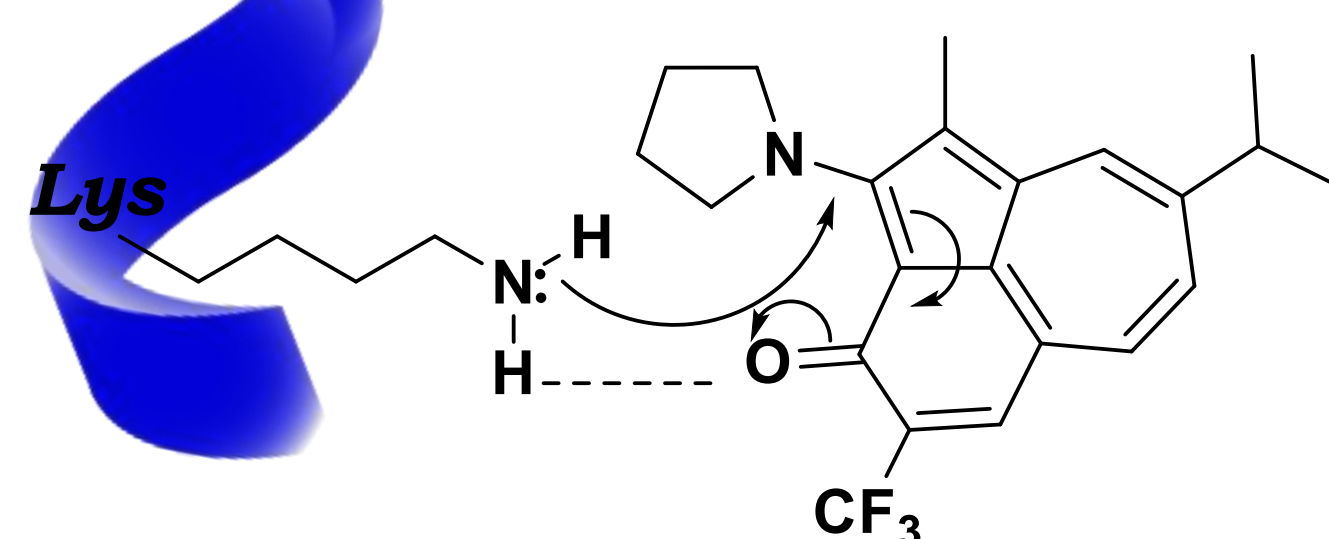
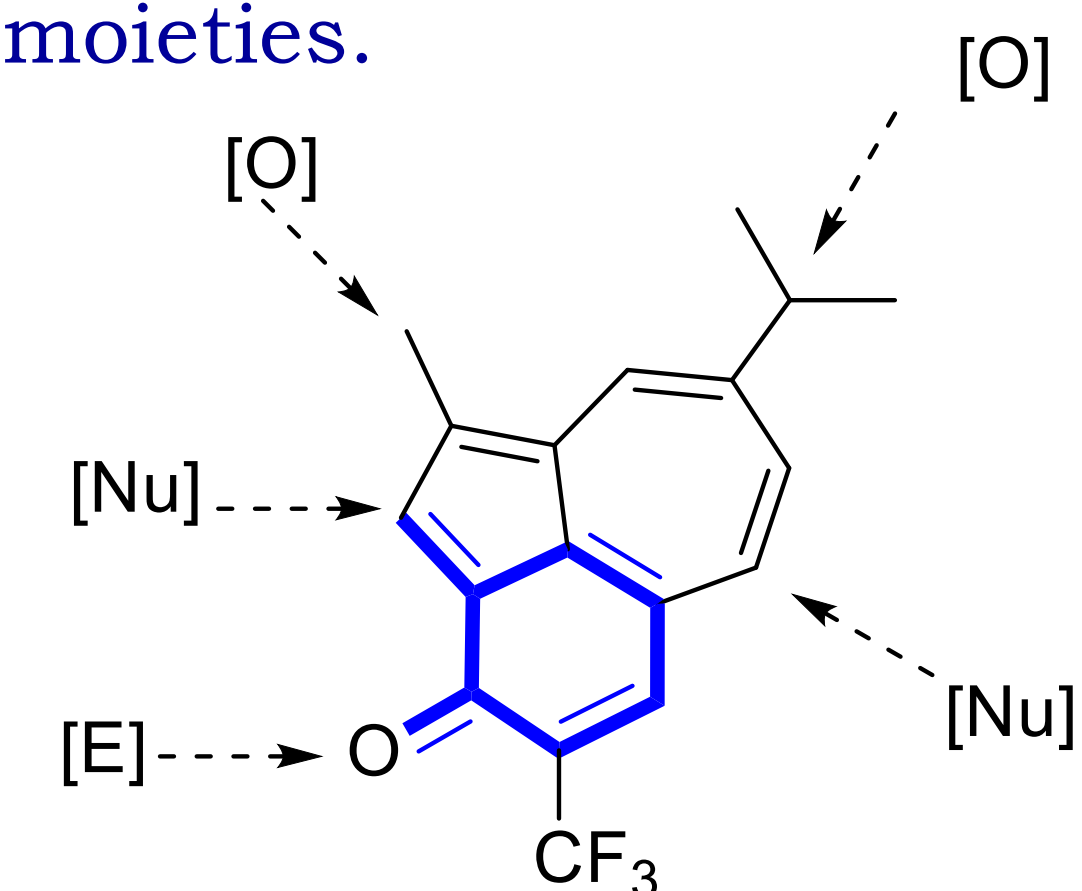
Benzazulenes

- Derived from natural product Guaiazulene.
- Fused three-ring azulene system.
- Exhibit selective inhibitory activity against Pim kinase family members.

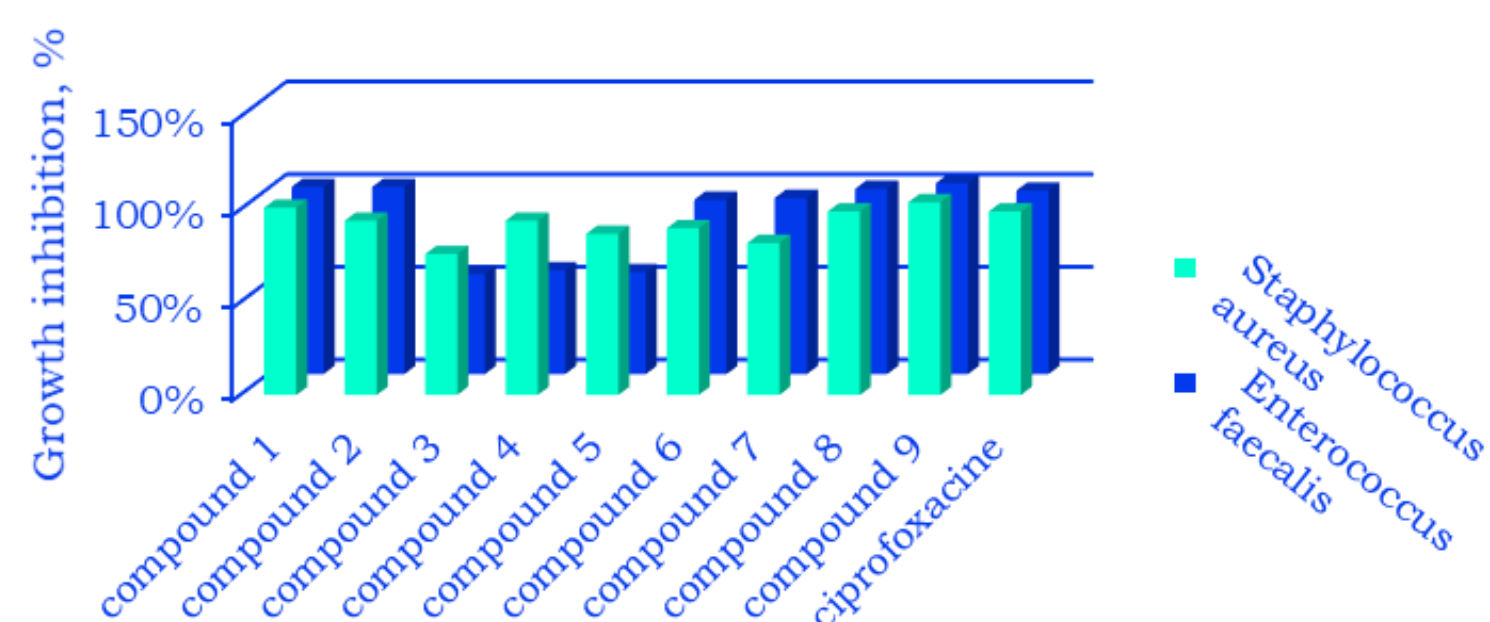
Anti-microbial resistance

- Urgent need of discovery and development of new antibiotics against resistance pathogens with clinical significance.

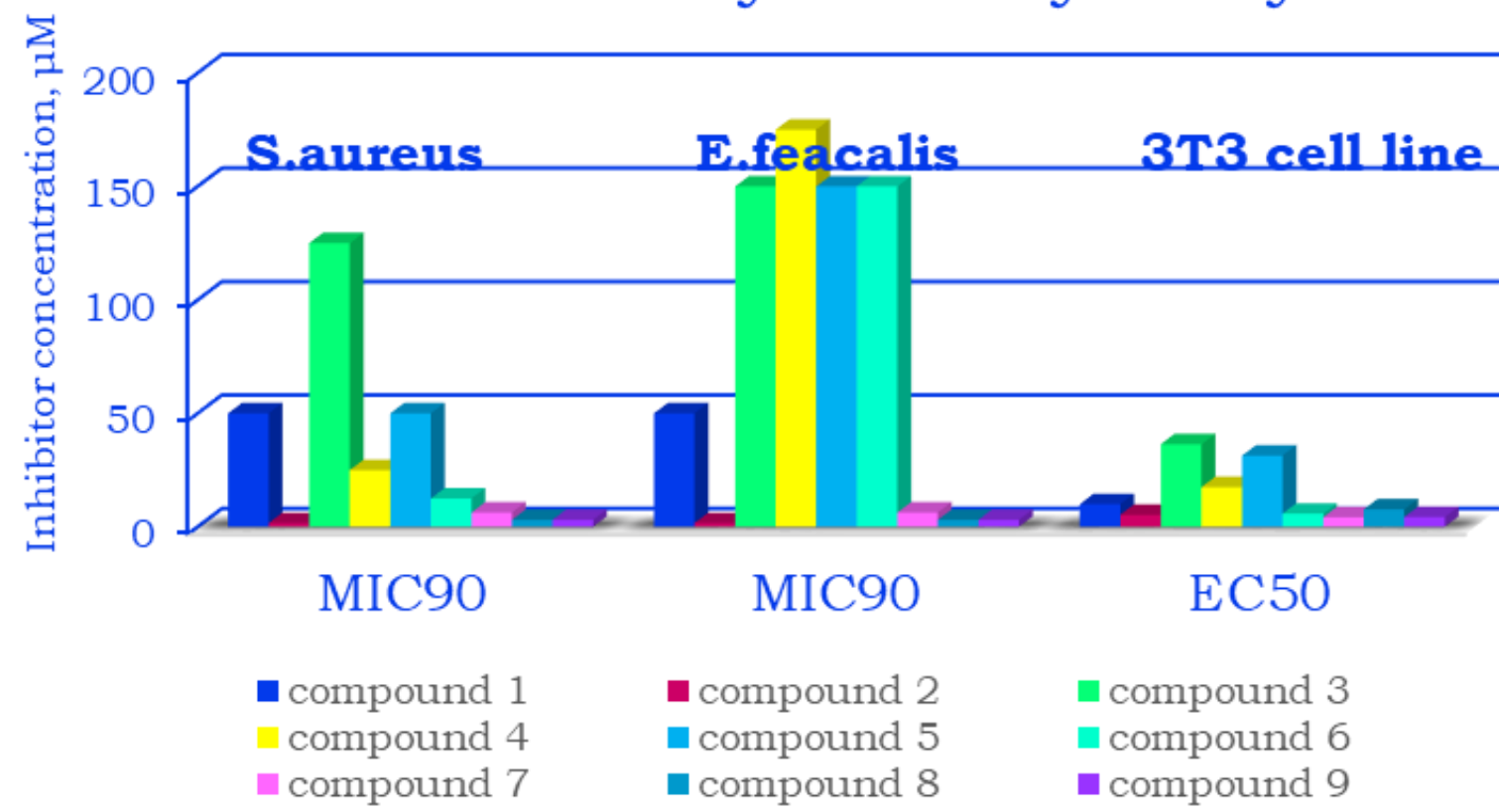
- Benzazulene scaffold can be diversely modified by oxidations and with nucleophiles & electrophiles.
- Embedded *o*- and *p*-quinone methide (QM) moieties.



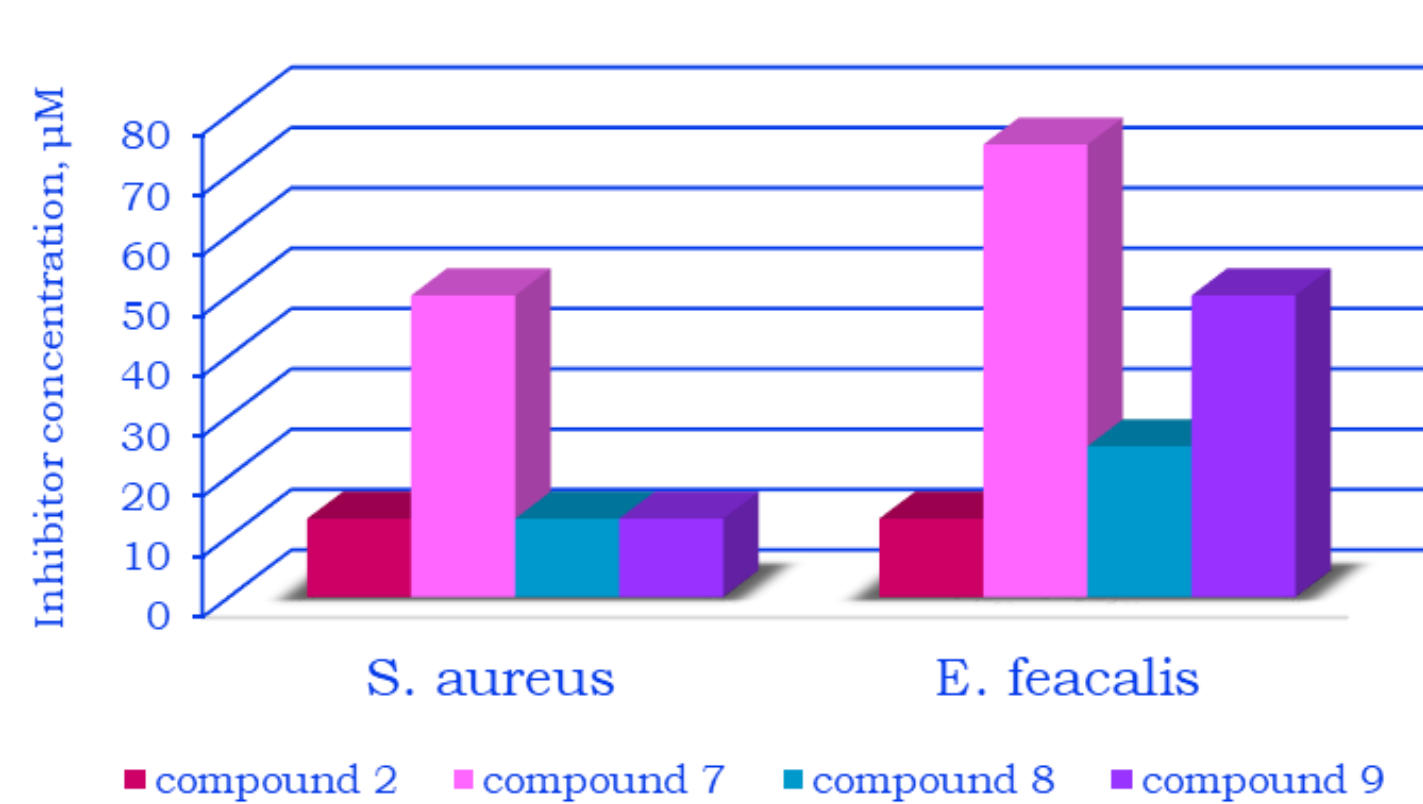
Screening assay



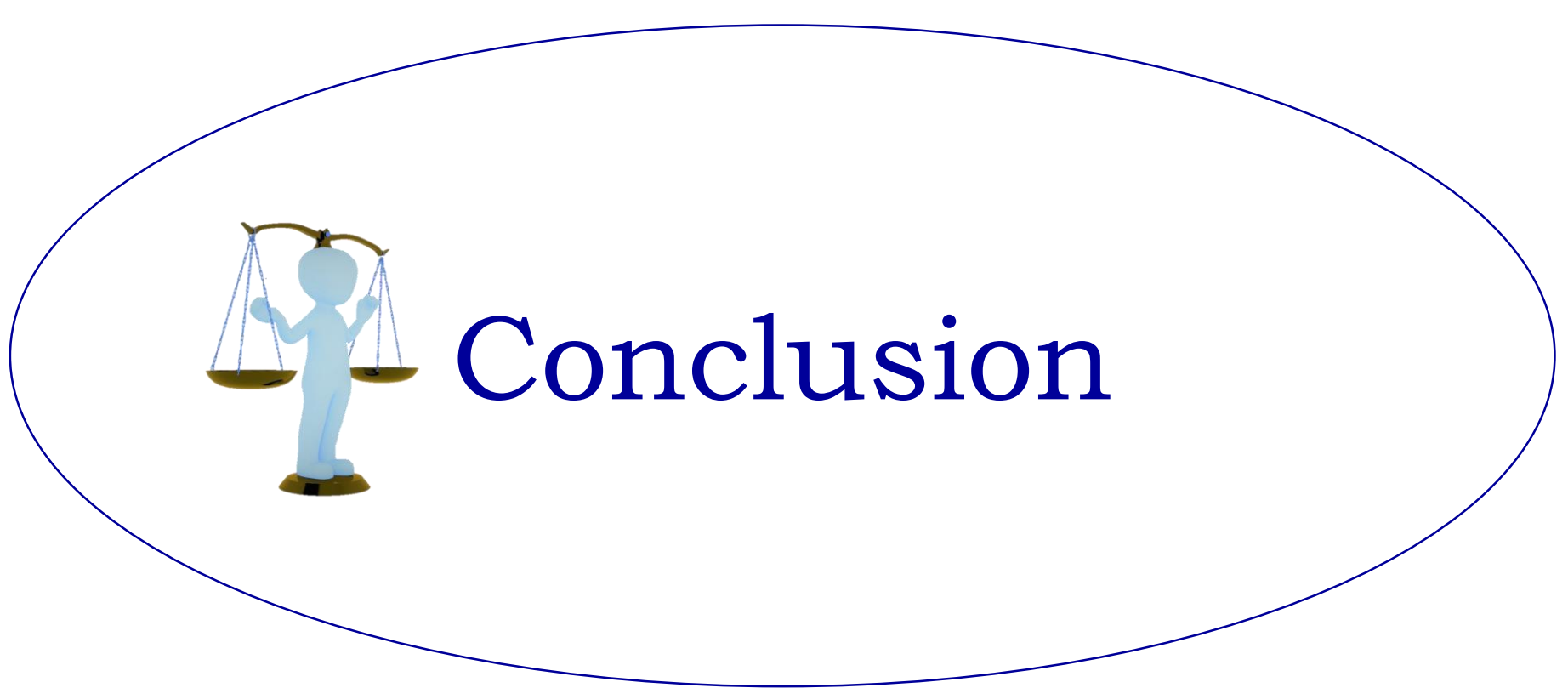
MIC and cytotoxicity assay



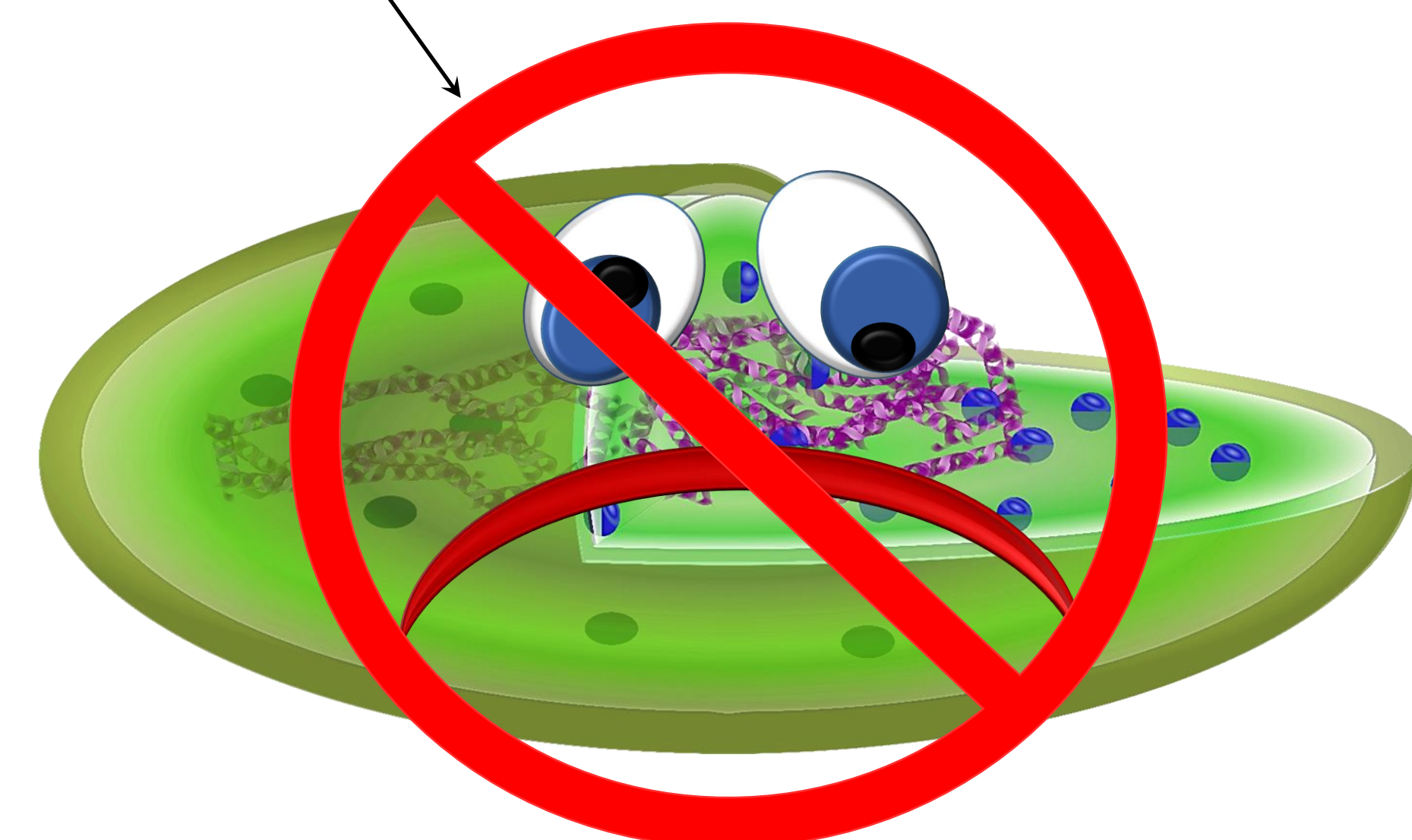
MBIC90



- **Anti-bacterial assays:** Screening assays, minimum inhibitory and bactericidal concentration determinations, minimum biofilm inhibitory concentration determination.
- **In vitro cytotoxicity**



- **Mechanism of action** (hypothesis): Intracellular reverse Michael reaction prevents bacterial growth and/or leads to bacterial dead.
- These compounds represent interesting and innovative leads with dual anticancer and antibacterial activity.



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References:

- 1) WHO: <http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/>
- 2) Aumüller *et al.*, Synthesis and Tautomerization of Benzo[cd]azulen-3-ones. *Organic Letters*. **2011**;13(7):1670-3.
- 3) Kiriazis *et al.*, Tricyclic Benzo[cd]azulenes Selectively Inhibit Activities of Pim Kinases and Restrict Growth of Epstein-Barr Virus-Transformed Cells. *Plos One*. **2013**;8(2).
- 4) Kiriazis *et al.*, Nucleophilic Substitution of Hydrogen Facilitated by Quinone Methide Moieties in Benzo[cd]azulen-3-ones. *Organic Letters*. **2017**;19(8):2030-3.