



Development of novel antiviroidal strategies: Towards drug discovery

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Introduction

- Viroids are the smallest known plant pathogens, composed of closed circular non-coding RNAs.
- They replicate autonomously inside host cells and trigger severe diseases in a wide range of crops.
- No effective treatments or control strategies are currently available.

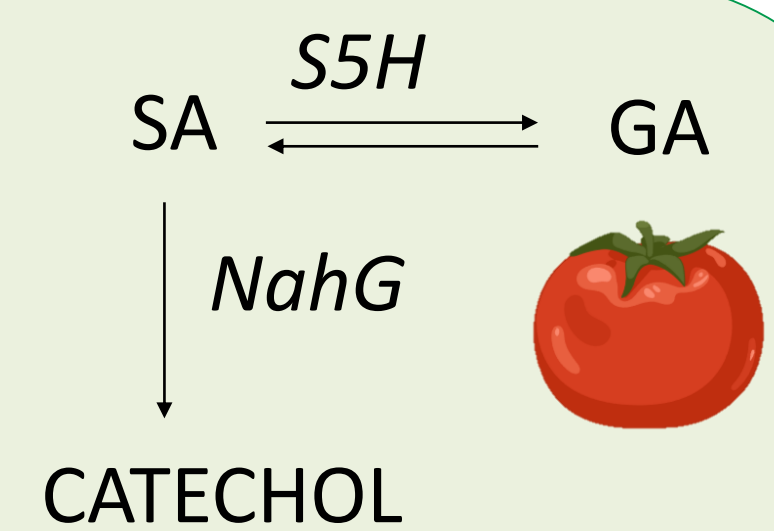


Promising candidates that
could be exploited as
antiviroidal drugs

State of the art

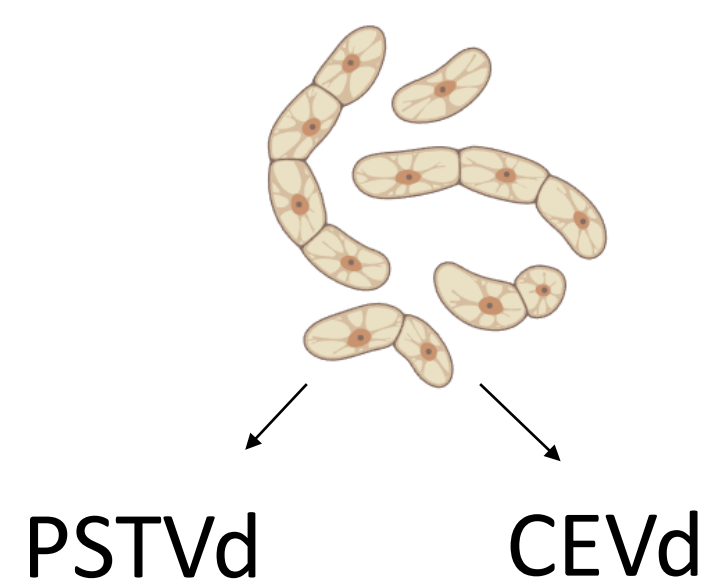
In our laboratory, we have demonstrated that several molecules contribute to tomato defense against viroids:

- **Salicylic acid (SA):** Key role in basal resistance. Tomato *NahG* lines are highly susceptible to CEVd (López-Gresa, 2016), while *RNAi_SIS5H* silenced lines are tolerant (Payá et al., 2022)
- **γ-aminobutyric acid (GABA)** induced by BTH: enhances resistance by reversing hypersusceptibility and activating defense genes (López-Gresa et al., 2019).
- **Polysome interaction blockers:** Viroids localize to ribosomes; targeting this may relieve viroid-induced ribosome stress (Cottilli et al., 2019).
- **Ethylene signaling modulators:** Reducing ethylene delays disease progression and eases ribosomal stress (Vázquez-Prol et al., 2020).
- **AZD8055** (TOR inhibitor): Restores autophagy and boosts tomato defenses, reducing PSTVd infection (Silva-Valencia et al., 2024).



Approach

1. Generate BY2-Vd cell system expressing PSTVd and CEVd



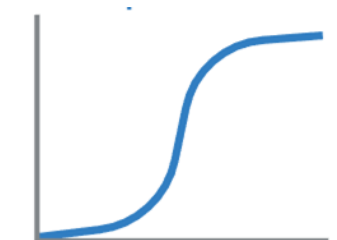
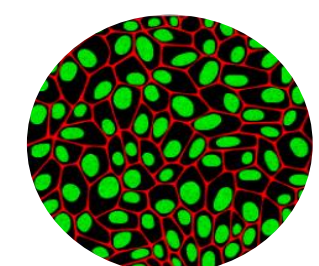
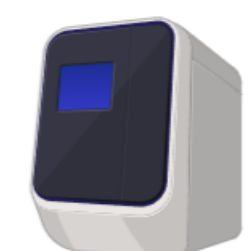
2. Screen compounds

- Salicylic acid
- GABA
- AZD8055
- Ethylene modulators
- Ribosome-targeting agents

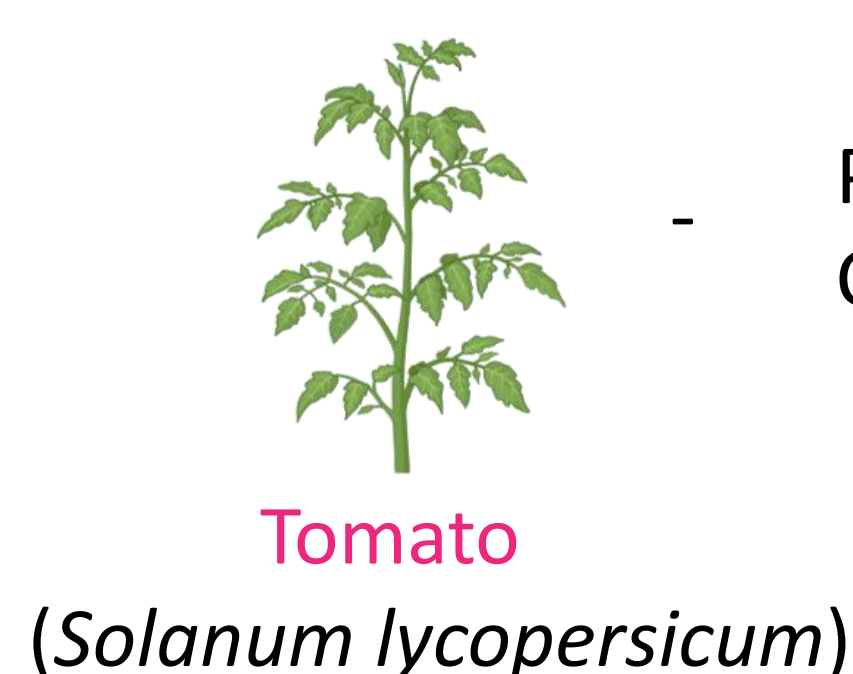


3. Evaluate effects

- Viroid accumulation (RT-qPCR, sRNA-seq)
- Subcellular localization (Microscopy)
- Host response (PR1, NAC82 expression)



In planta validation



- PSTVd
- CEVd

Pospiviroidae family



- PSTVd



Chrysanthemum
(*Chrysanthemum morifolium*)

- CChMVd

Avsunviroidae family

Research goals

- Establish a BY2 cell-based system to screen and identify compounds with antiviroidal activity.
- *In planta* validation of candidate compounds in diverse hosts and viroid families.
- Demonstrate the mechanistic basis of action.
- Contribute to future crop protection solutions against emerging viroid threats.