# Lysis inhibition

### Structural basis of lysis inhibition

Holin is the controller of phage-induced rapid-lysis and initiation of cell-wall digesting activity. Lysis can be understood through genes t and e, which control holin and endolysin. LIN requires consideration of r genes too. rI and rIII expression lead to an inhibition of the holin protein, they are antiholin**.** So the RI plays a role in secondary adsorption signal transduction to protein T, while RIII together with RI together serve to stabilize the not-yet hole-forming form of protein T.RI is periplasmic and it is labile in that environment. However, it can change to its stable conformation due to secondary adsorption, which can then inhibit T-hole formation.RIII is a cytoplasmatic protein and it is suggested to stabilize the complex of RI-T.

* **Our model:** We have the timer molecules that “reproduce” and when they arrive to a certain number n the cell lyses. The number of this molecules only starts to rise after the first infection. We could say that our timer molecules count the time until the T-holin can eventually make the cell lyse.

When a superinfection occurs, then it delays the time of lysis 5 or 10 minutes. And the time of the first superinfection also delays lysis but not very significantly. So if we set n = 6, then it means that normal lysis without superinfection occurs when there are 6 timer molecules. What we can do is that when there is a superinfection, the number of timer molecules is reduced by 2 units.

When there has been a superinfection, the T-holin protein is inhibited and forming a stable complex. Also, all the processes related to the rapid-lysis decrease their rate: for example, during rapid lysis there is some ATP leak which rate is decreased when there is a superinfection. So maybe the solution might be reducing the birth rate of the timer molecules.

Also, there are some hypotheses that say that the rate of superinfections can limit the efficiency of lysis inhibition. This can be due to the fact that the system cannot recognize to subsequent superinfections as discrete stimuli.

**How many superinfections can a cell support?** I have not found any experimental evidence about that. However I have read that what lysis inhibition does is delay and lower the rate of all the processes that occur during rapid lysis. Therefore, at some point, the cell dies eventually anyway and it may depend on the health of the cell before getting infected.

I have also read that the free RI proteins adhere to the N terminal of the T Holin that has a SAR (signal anchor release) site that can transport them to the periplasm (then they adhere to the T terminal which is located in the periplasm). Free RI crystalizes and those structures act as a sink for released RI proteins from the RI-T complex. The transport to the periplasm by SAR confers proteolytic instability of RI. Then Antiholin RIII adheres to the N terminal to stabilize the complex RI-T. (REFERENCE 10 CHEN AND YOUNG)

In a more recent study (REFERENCE 13) supports the fact that RI is very unstable: its SAR domain is recognized by periplasmic protease DegP resulting in rapid degradation of RI. In this scenario, in response to superinfection the RI gets stabilized and therefore there is more available RI, which would bind to the periplasmic site of T and prevent it from making holes. They have found that the signal that stabilizes RI is the DNA of the superinfecting phage. It gets degraded rapidly, but if it binds to the RI-T complex it can stabilize it.

( 🡪 The more superinfections, the more RI there will be and the more free RI there will be (because all the T Holins will already be in an RI-T complex and stabilized)). Therefore all the free RI can be attached to the crystals and no longer be used to delay lysis inhibition (?)