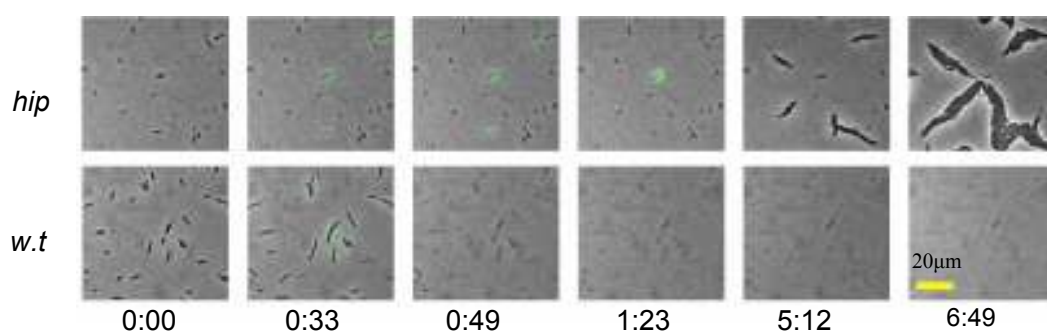


## Non-Genetic Individuality in the Host-Phage Interaction

Non-genetic individuality has been implicated in a wide range of biological processes such as differentiation and stress response. For example, sub-populations of bacteria can persist extensive antibiotic treatments. We previously showed that persistent bacteria are generated upon starvation (Type I) or continuously (Type II), and enter a slow growth state that protects them from the lethal action of antibiotics. Our goal was to study the effect of Type I persistence on the interaction between *E.coli* and the lambda phage, during prophage induction or infection by phages that do not form lysogens. We found that Type I persisters are protected from reversible prophage induction (Fig 1). However, they are not protected from infection. Long-term monitoring of single-cell fluorescence in infected bacteria carrying *gfp* fused to lytic promoter revealed that phages do not express lytic genes during the persistent state. When persister bacteria switch to normal growth, the phage resumes the process of gene expression that ends up in lysis. Using a simple model for the host-phage interaction, we found that the observed non-genetic individuality can alter the outcome of population dynamics, and might be relevant for understanding the co-evolution of bacterial hosts and phages. Our results shed new light on the dormancy of persister cells and suggest phage therapy as a specific line of attack for fighting persistent bacterial infections.



**Fig 1: Time-lapse microscopy of *w.t* and high persistence (*hip*) strains carrying heat inducible prophage, during and after heat induction.** The activation of the phage lytic pathway was monitored by measuring the fluorescence level of GFP expression under the control of the phage lytic promoter. At  $t=0$ , the lysogenic bacteria are exposed to 42°C for 80 min. Then, the temperature is set to 32°C. At the end of the measurement no survivors are observed in the *w.t*, while a number of dividing cells can be seen in the *hip* strain. These results show the correspondence between persistence to antibiotics and to prophage induction.