

Exploring the role of activating transcription factor 6 in Kaposi's Sarcoma associated-herpesvirus infection

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CSEP

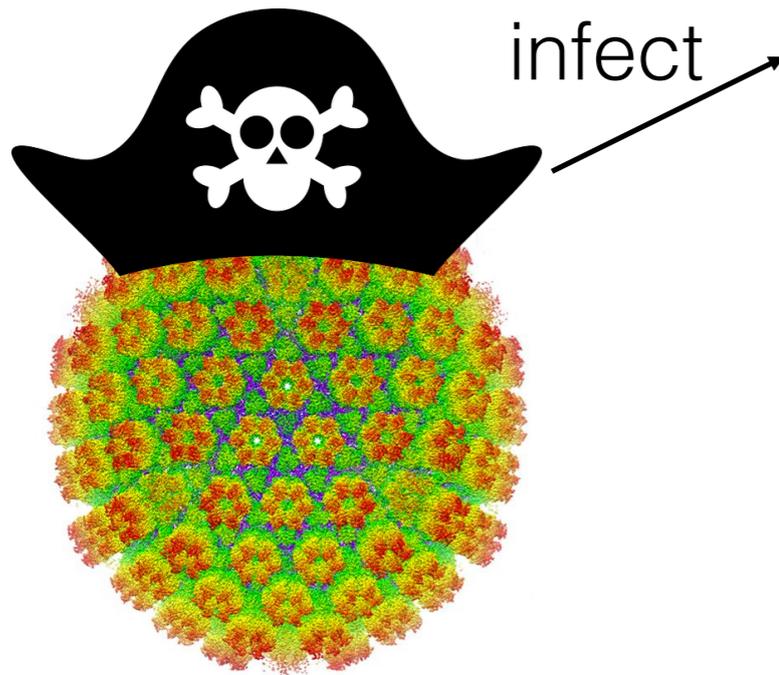


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Finding ways to attack pirates of the human body



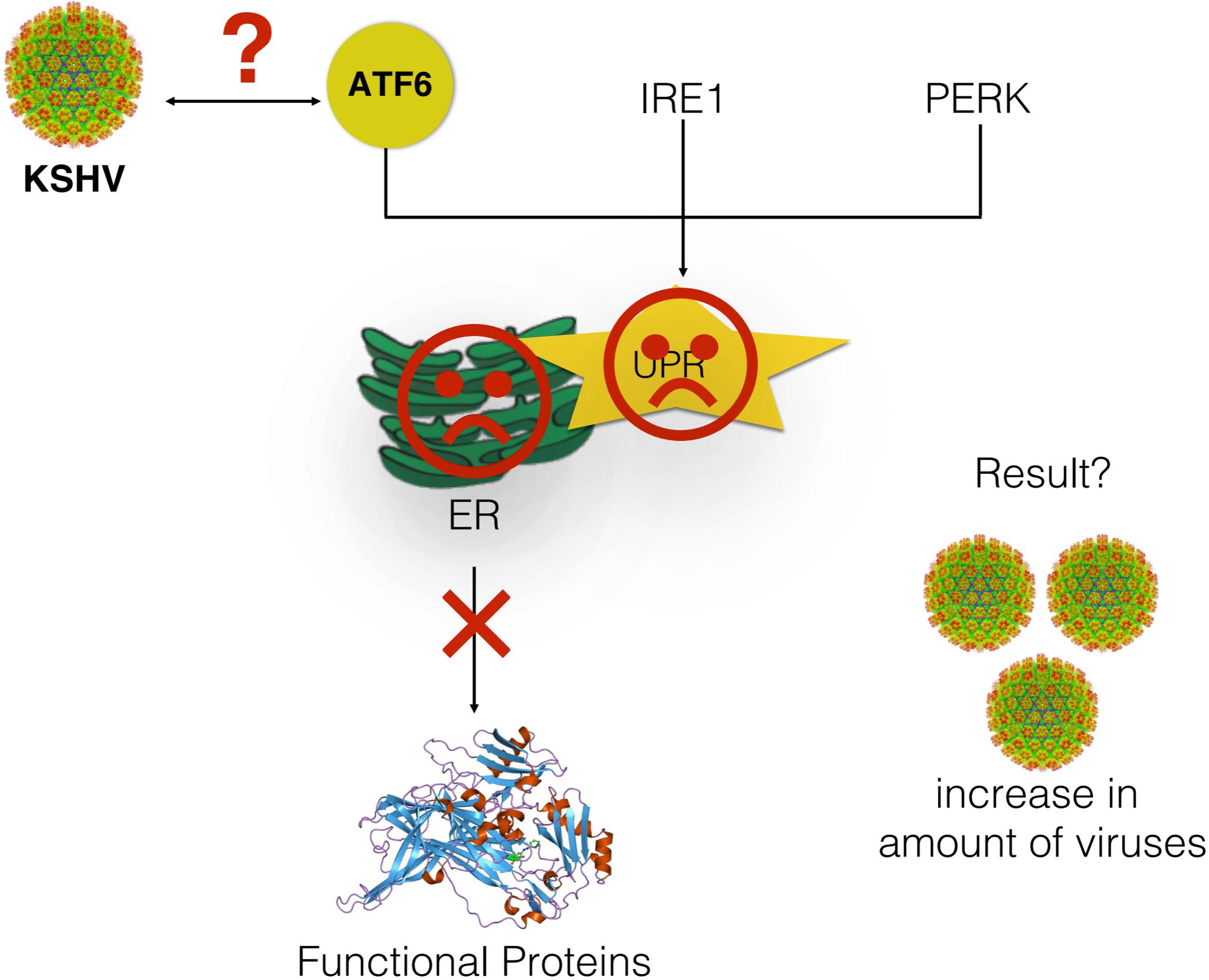
Kaposi's Sarcoma
cancer

study

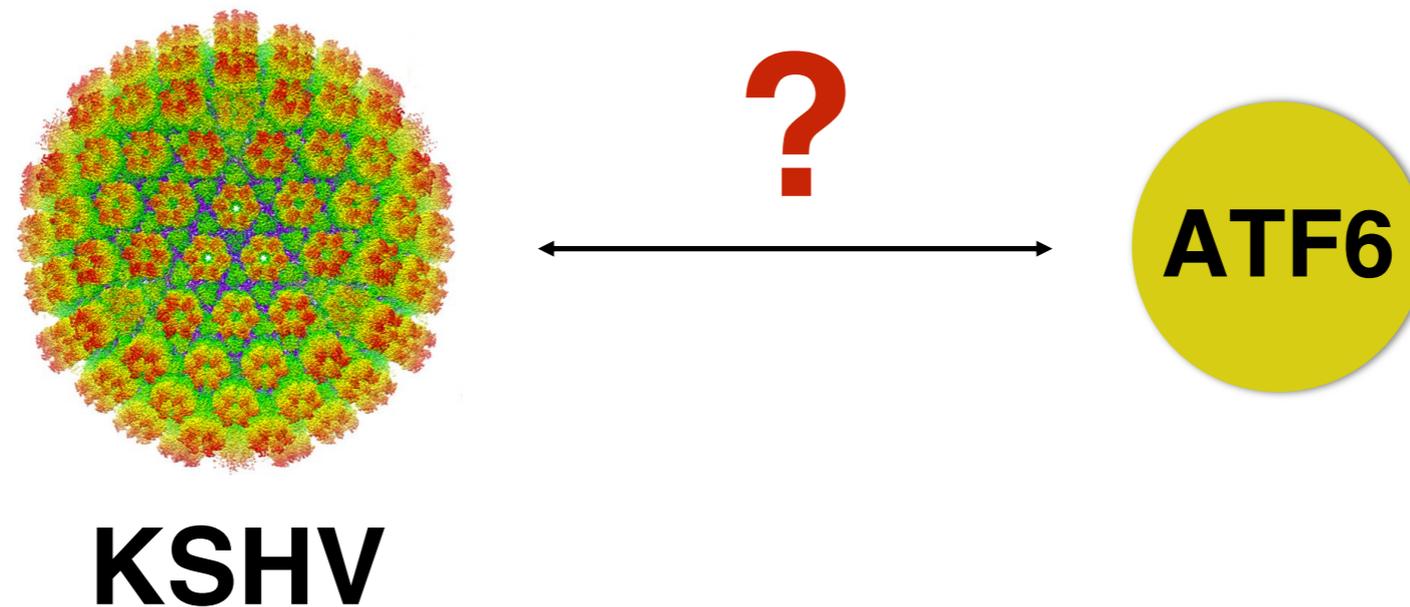


- Understand virus-host interactions
- Find targets for the development of future therapies

Understanding role of ATF6 in KSHV infection

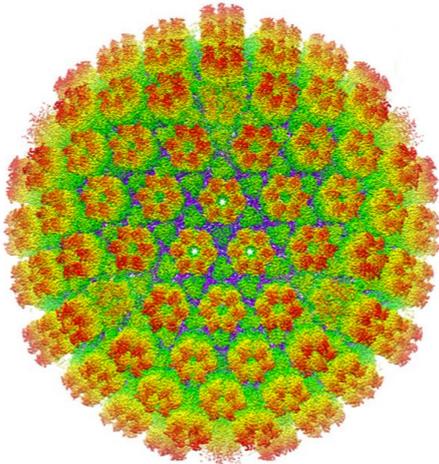


Understanding role of ATF6 in KSHV infection

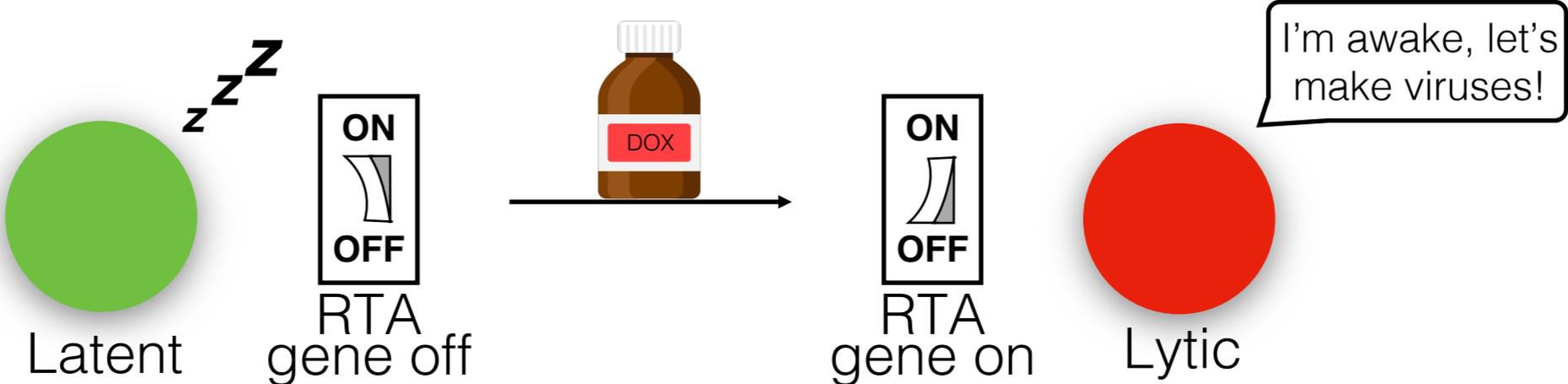


How does KSHV modulate the ATF6 pathway to its advantage?

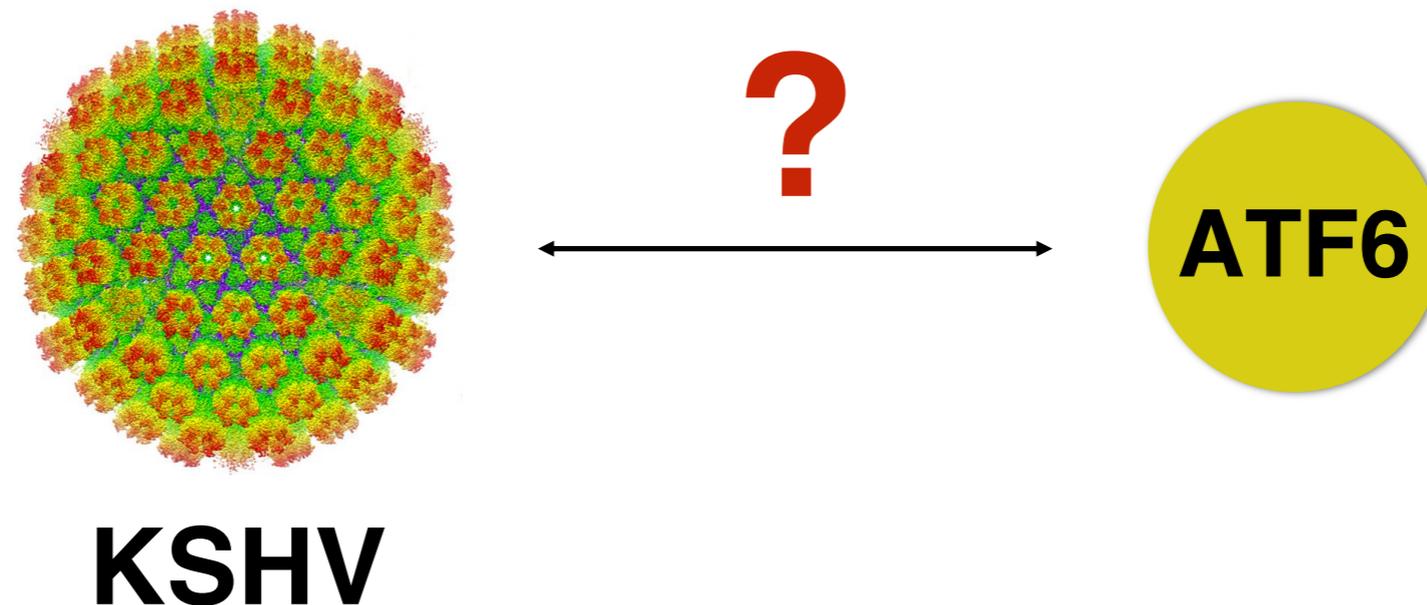
Understanding role of ATF6 in KSHV infection



KSHV



Understanding role of ATF6 in KSHV infection



How does KSHV modulate the ATF6 pathway to its advantage?

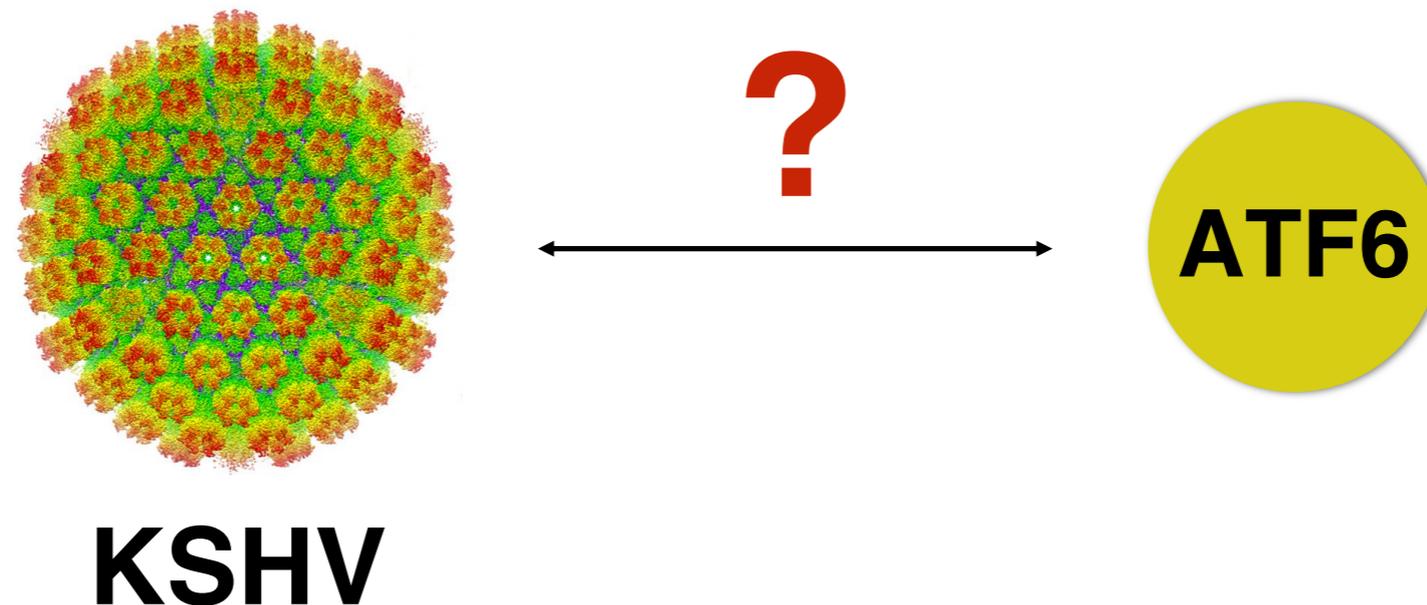
Understanding role of ATF6 in KSHV infection



ATF6

- Protein that acts like a signal in the cellular stress response known as the unfolded protein response (UPR)
- Signals for other proteins to relieve the stress in the cell

Understanding role of ATF6 in KSHV infection



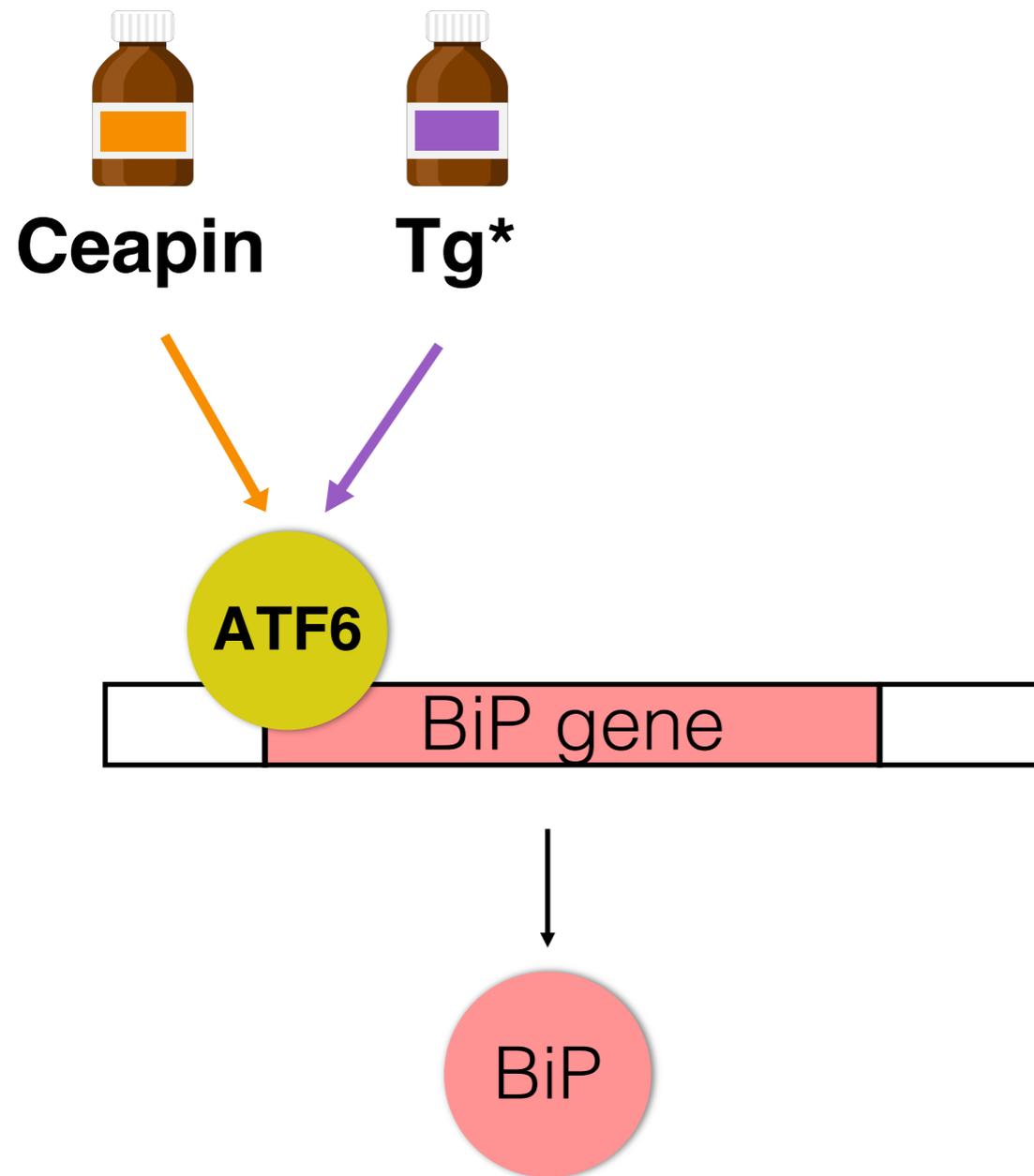
How does KSHV modulate the ATF6 pathway to its advantage?

Chemically controlling ATF6 with Ceapin



- To test ATF6s' role in KSHV infection, we used a drug, known as Ceapin
- It prevents ATF6 from reaching its location to do its job

Chemical controls of ATF6 activity in cells



What are the protein levels of BiP in cells treated with Tg, Ceapin or both?

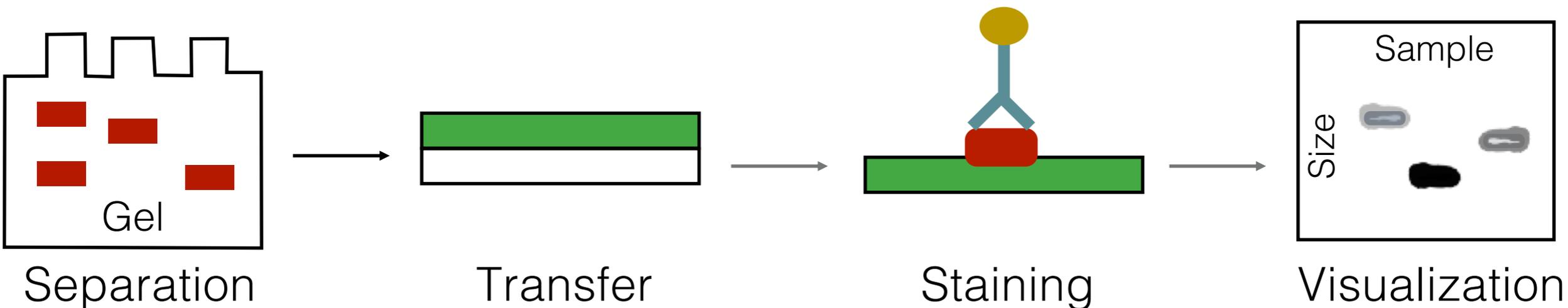
Tg ↑ BiP

Ceapin ↓ BiP

Ceapin+Tg ↓ BiP

Tg* = Thapsigargin

How to detect proteins in cells: perform a Western Blot

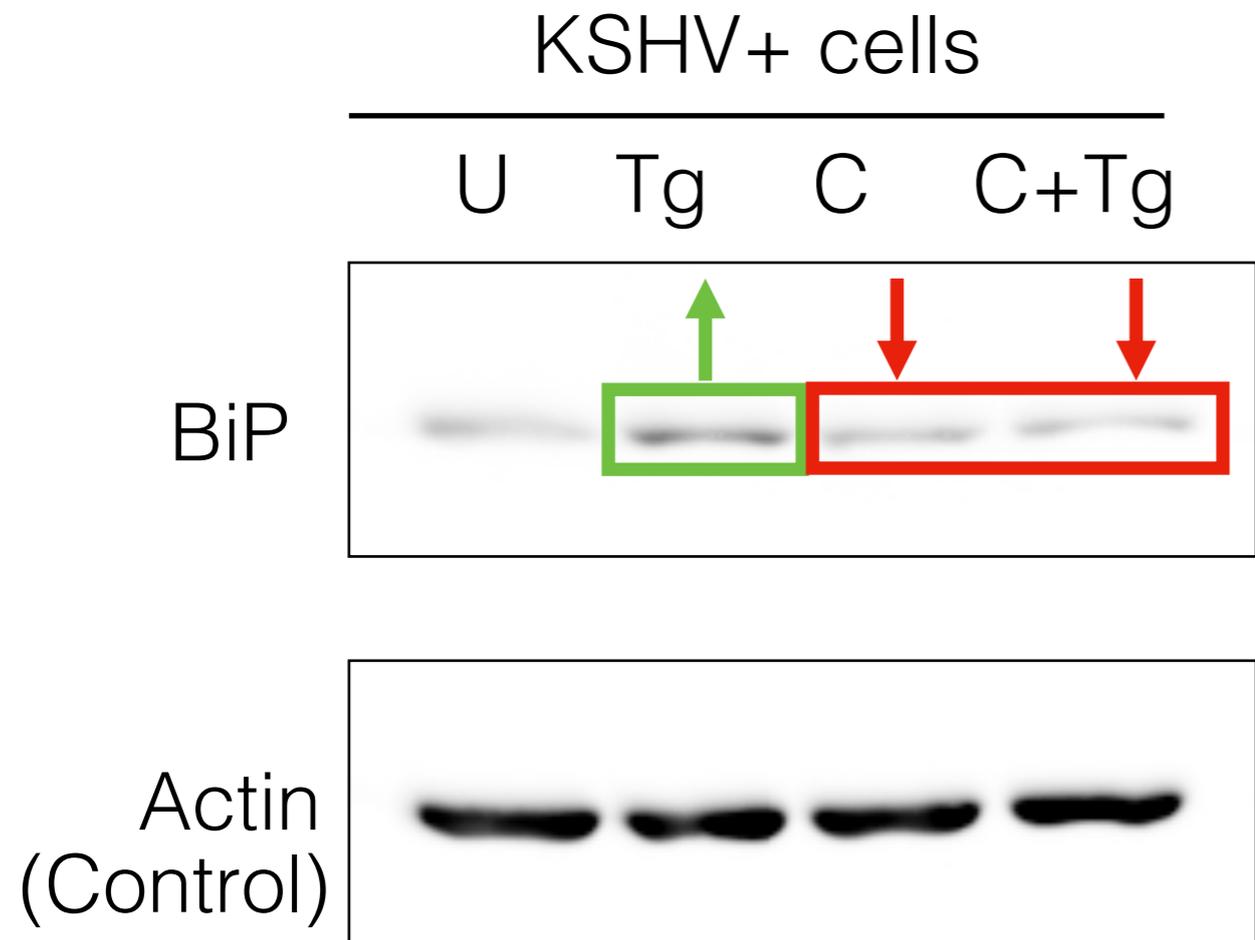


- The darker the band, the more protein.

Ceapin prevents up regulation of BiP

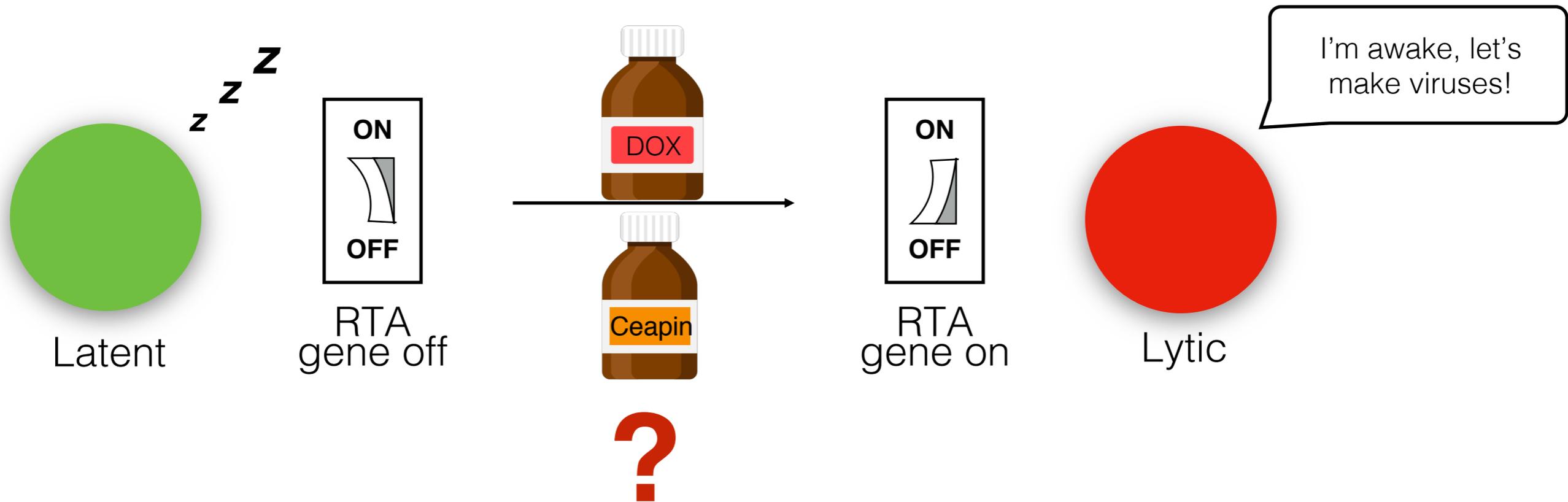
Legend

U: Untreated
Tg: Thapsigargin
C: Ceapin
C+Tg: Ceapin + Thapsigargin

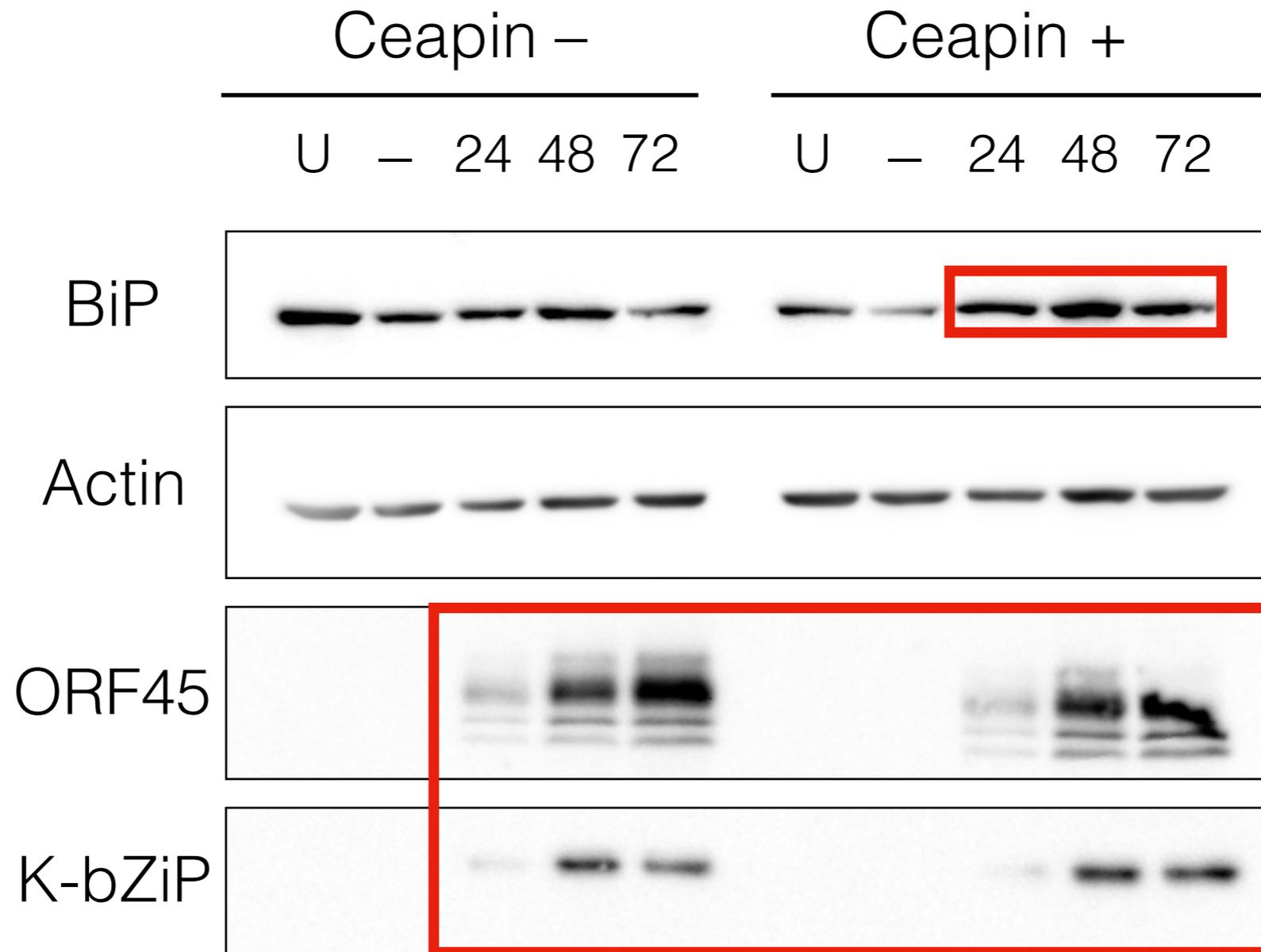


- Ceapin prevents ATF6 from reaching BIP gene
- As a result, there is no up regulation of BiP

Testing lytic cycle with Ceapin treatment

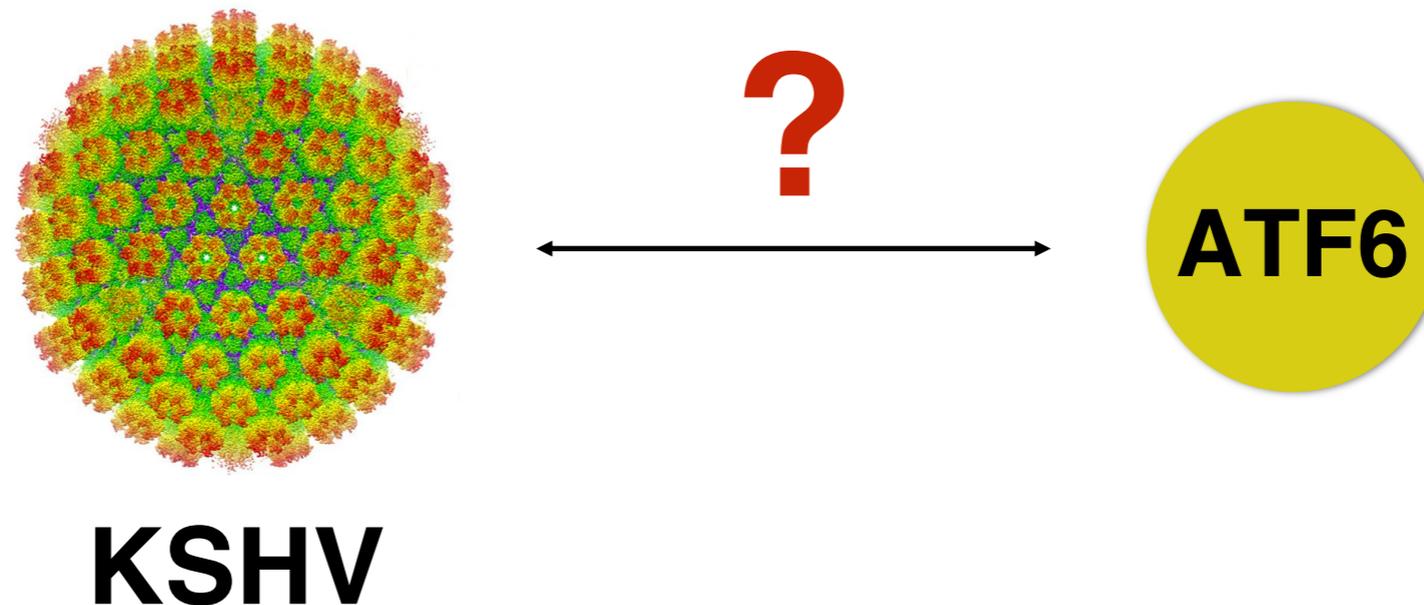


Ceapin does not prevent viral reactivation



- ORF45 and K-bZiP are proteins expressed in the lytic cycle of KSHV
- There appears to be no change in viral reactivation with Ceapin treatment

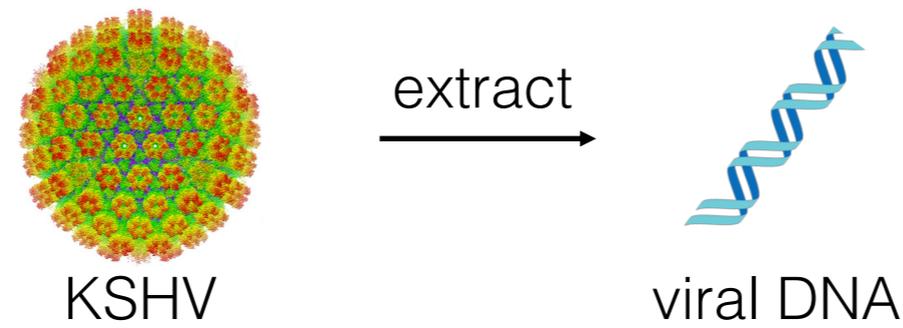
KSHV reactivation is independent of ATF6



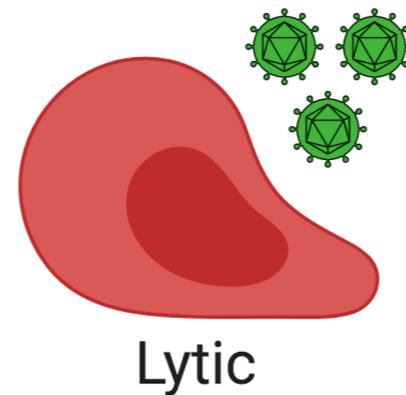
In cells that contained lytically active KSHV and were treated with Ceapin, viral protein production remained the same, indicating that inhibiting ATF6 does not prevent viral production.

Analysis of other ATF6 targets and viral DNA to be done

- Study viral DNA synthesis during active viral replication in cells treated with Ceapin



- Study virus production in cells treated with Ceapin



Acknowledgements



Dr. Carolina Arias



Guillermo Najarro

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*“The single biggest threat to man’s continued dominance
on the planet is the virus.”*

— Joshua Lederberg, Ph.D Nobel Laureate
