

Artemisinin regulation of Androgen Receptor in Prostate Cancer cells

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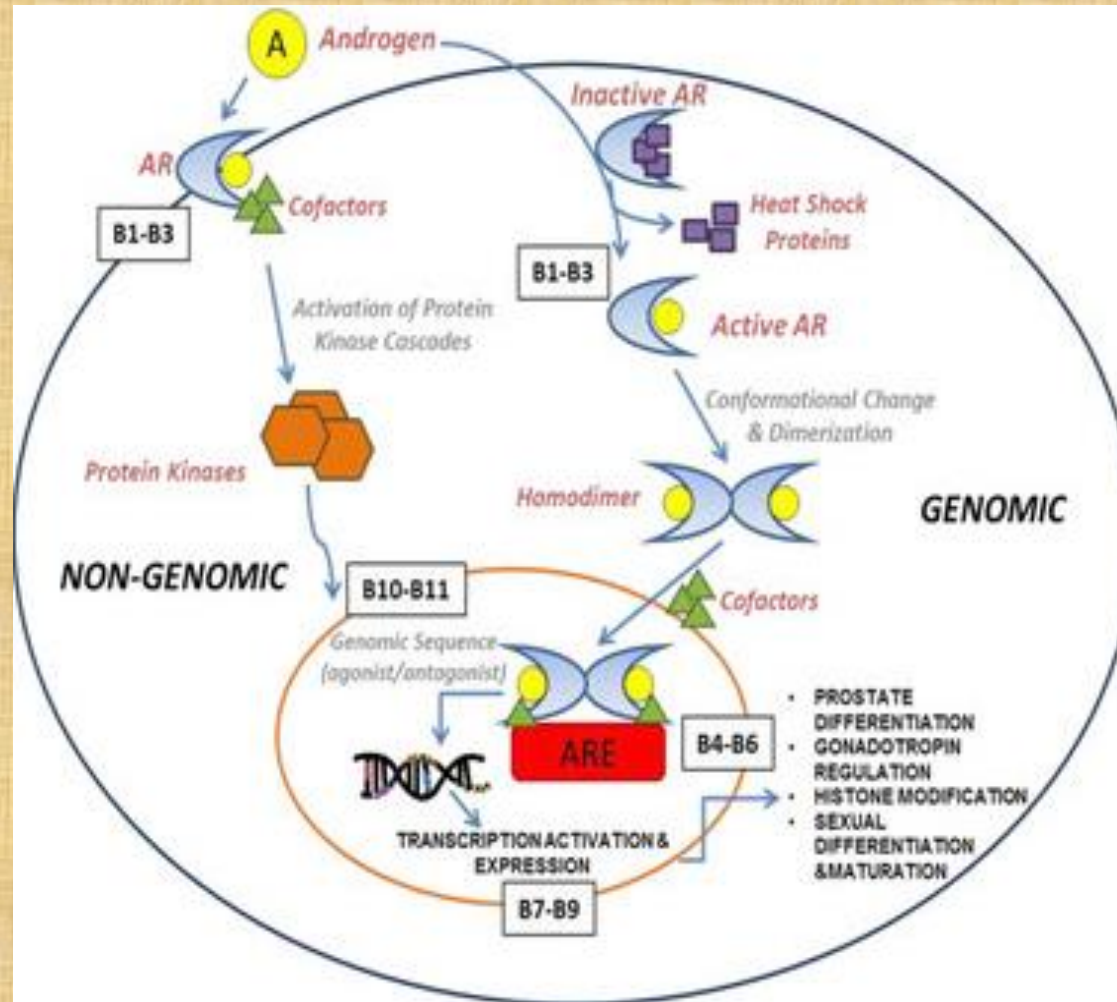
Prostate Cancer

- Most common cancer among males in the western world
- Can be diagnosed as a hormone dependent malignancy
- Can progress to become hormone independent
- Current therapy includes chemotherapy, radiation, hormonal therapy
- Produce many undesirable effects in the patient
- No single therapy exists that can prevent progression effectively with minimum side effects

Androgens and Prostate cancer

- Androgens are essential to the development and maturation of the prostate gland
- Androgens stimulate cell proliferation of prostate cancer cells in culture
- High levels of androgens associated positively with prostate cancer incidence
- Orchidectomy associated with high levels of protection against prostate cancer

Androgen Receptor Signaling





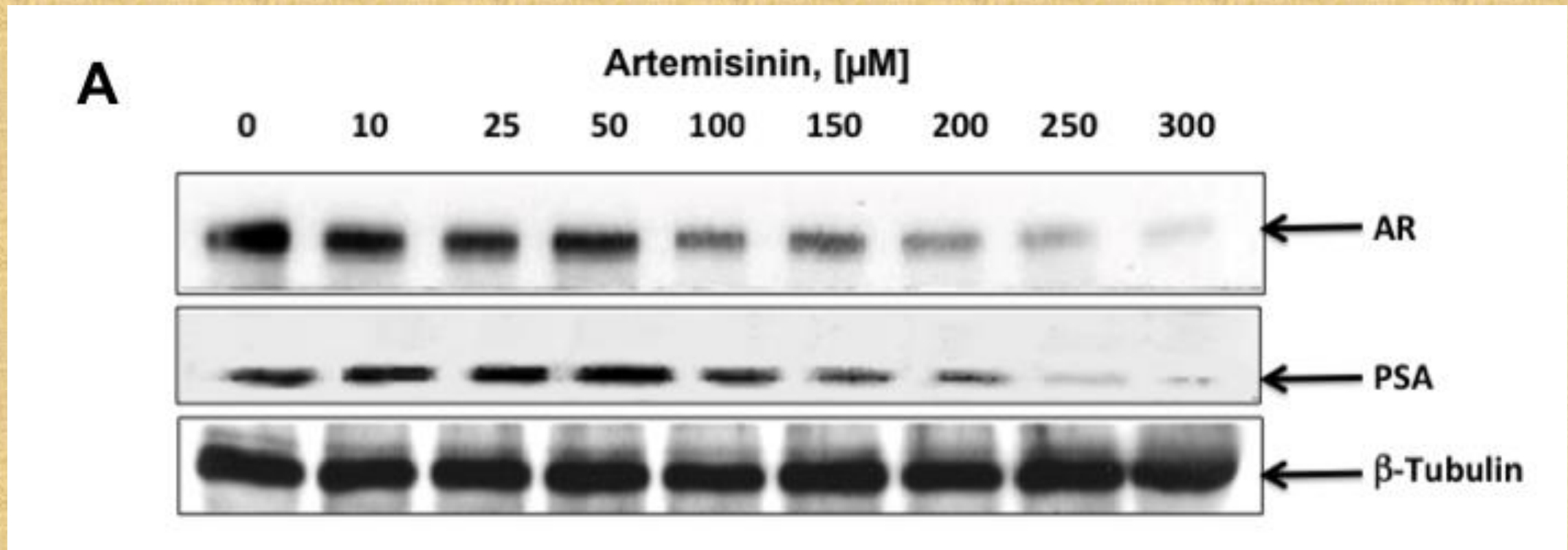
Artemisinin

- A sesquiterpene lactone from *Artemisia annua* plant already in use for malaria treatment
- Chinese have used this for over 2000 years as a remedy for fever and other ailments
- Has been shown to be effective against many types of human cancer cells in culture and in mice
- Causes a major halt in the cell cycle of cancer cells and arrests them in the G1 phase of the cell cycle

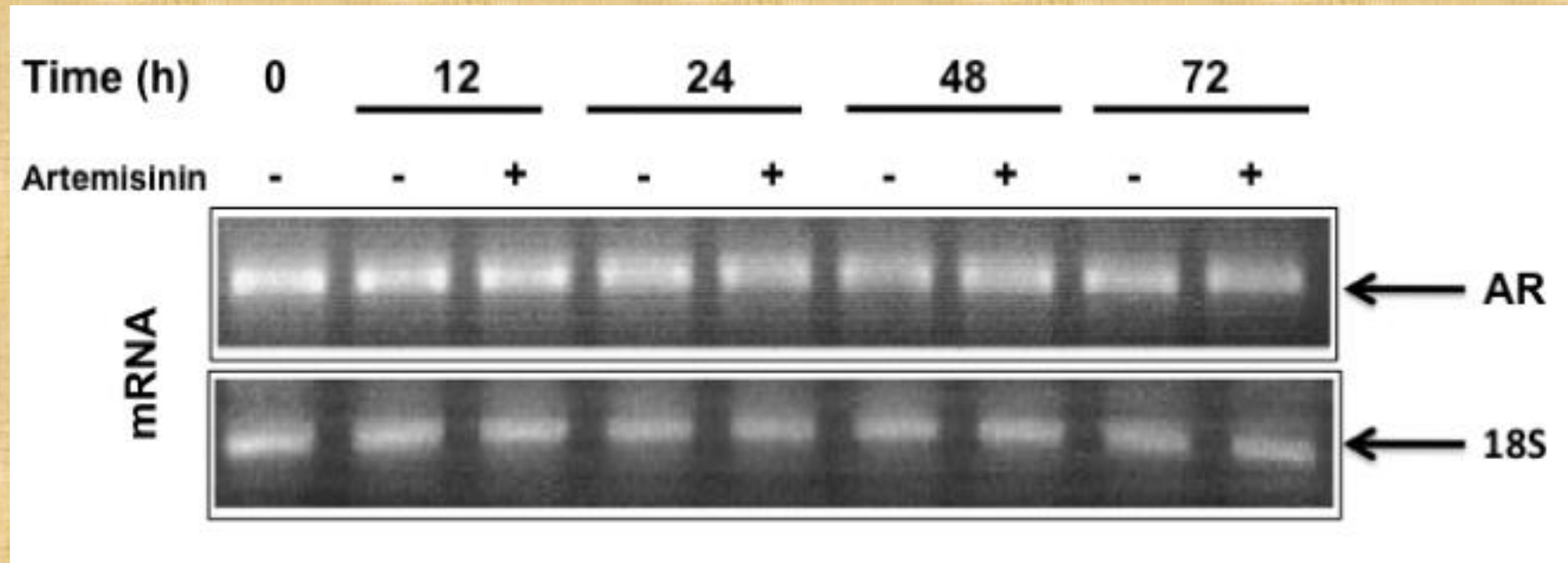
Research Question

- Artemisinin causes growth inhibition in prostate cancer cells (LNCaP) in culture. Does artemisinin affect androgen sensitivity of these cells?
 - *Test to see if artemisinin is effective against addition on androgens in terms of growth inhibition.*
 - *Cells without any treatment*
 - *Cells with artemisinin*
 - *Cells with androgen*
 - *Cells with both treatments*

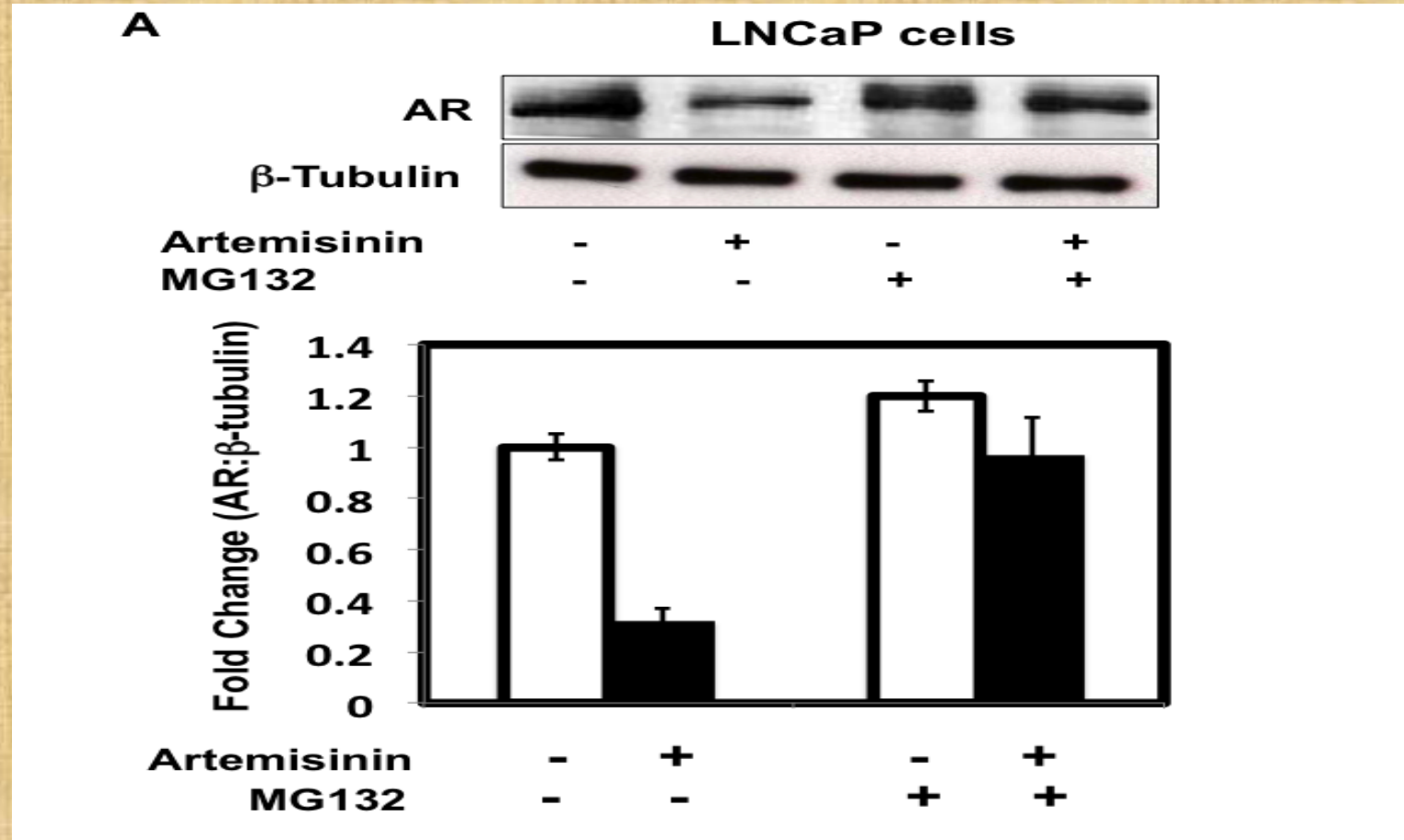
Artemisinin causes functional AR levels to drop in LNCaP cells



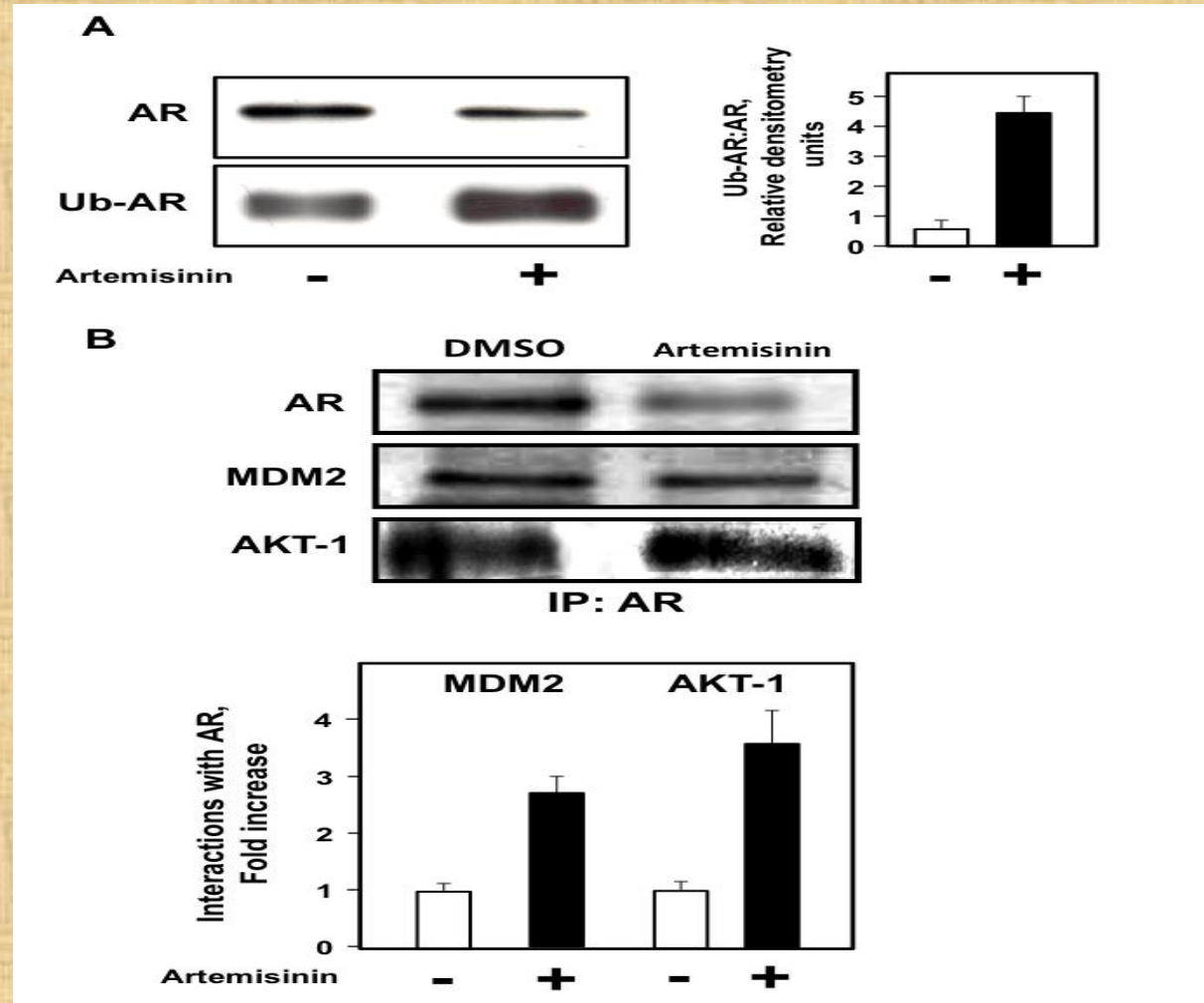
No change in mRNA levels so regulation is not at the transcriptional level



MG132 blocks protein degradation in cells



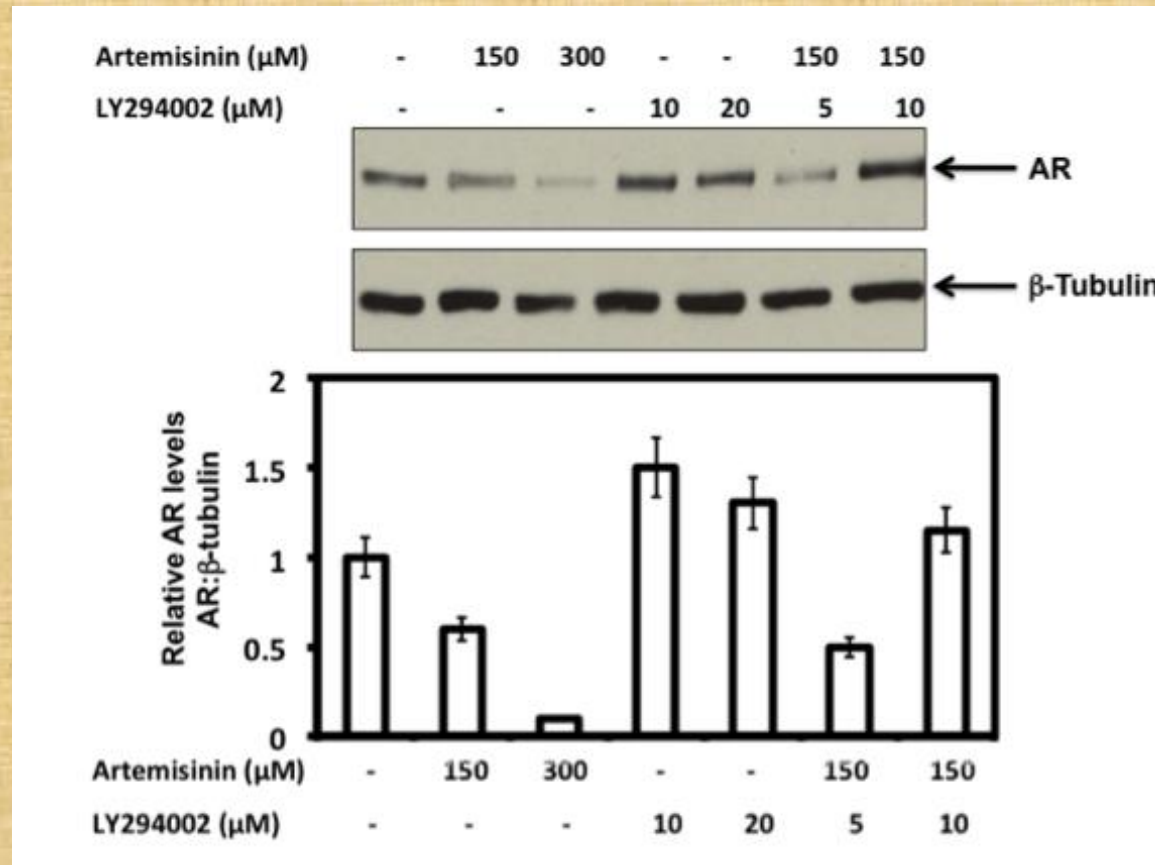
Increased level of ubiquitinated AR under ART treated conditions. Increased association with AKT, an enzyme that helps degrade AR protein



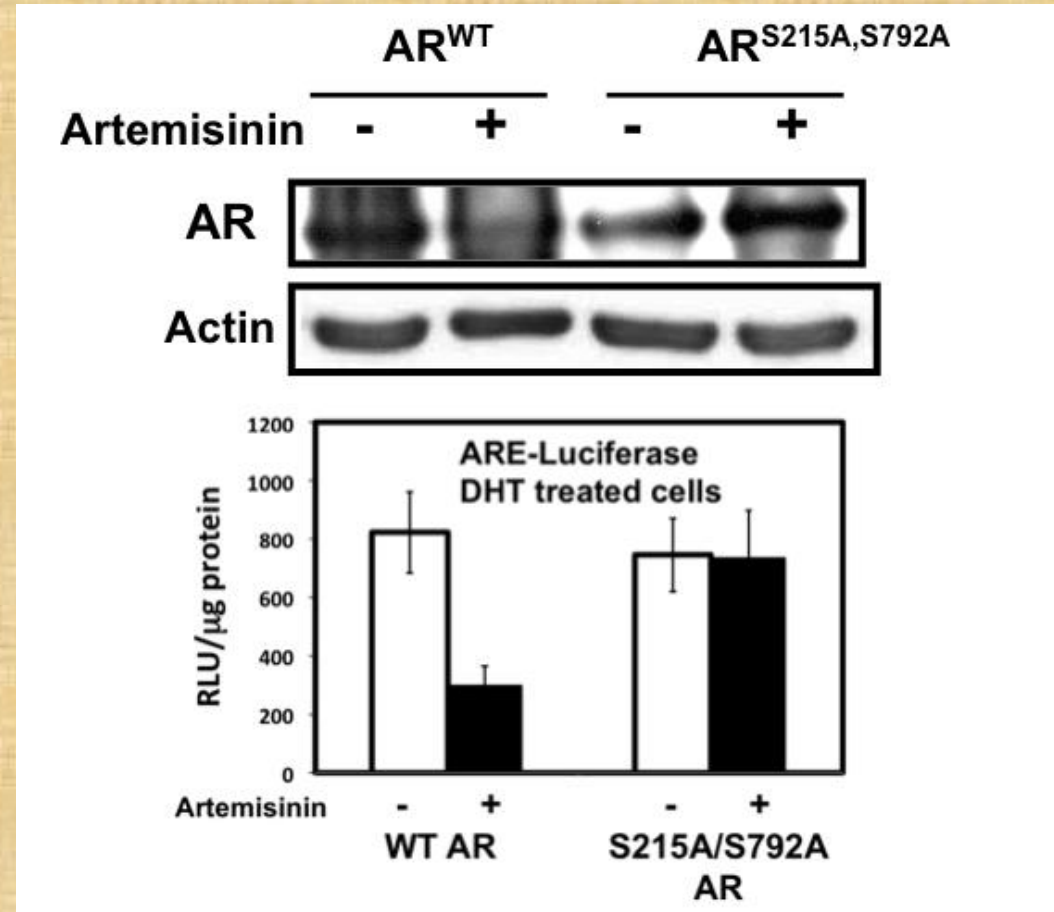
ART increases AKT activity in cells



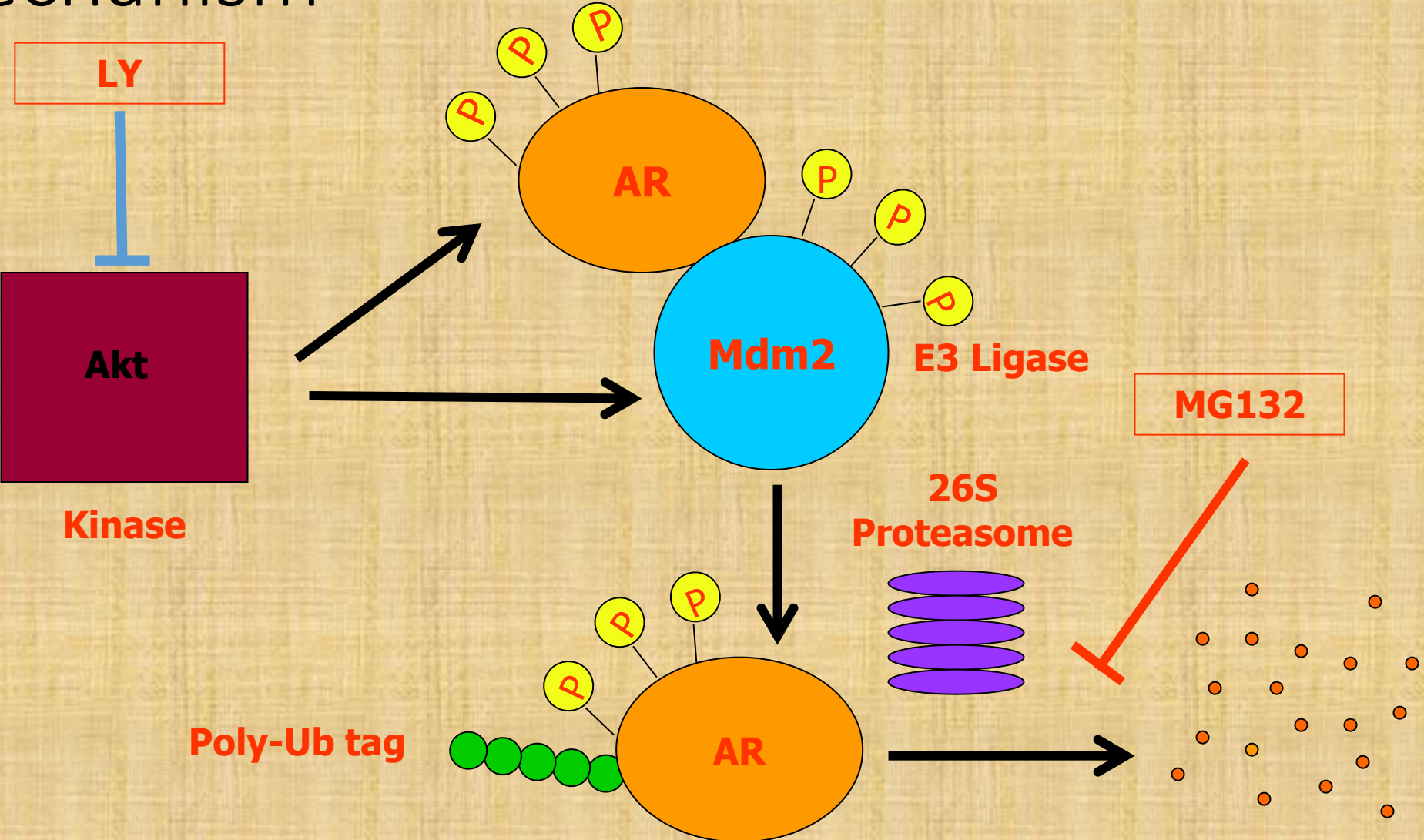
LY is an AKT inhibitor and reverses Art mediated AR degradation



AR mutant at critical amino acids is not degraded due to ART



Mechanism



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