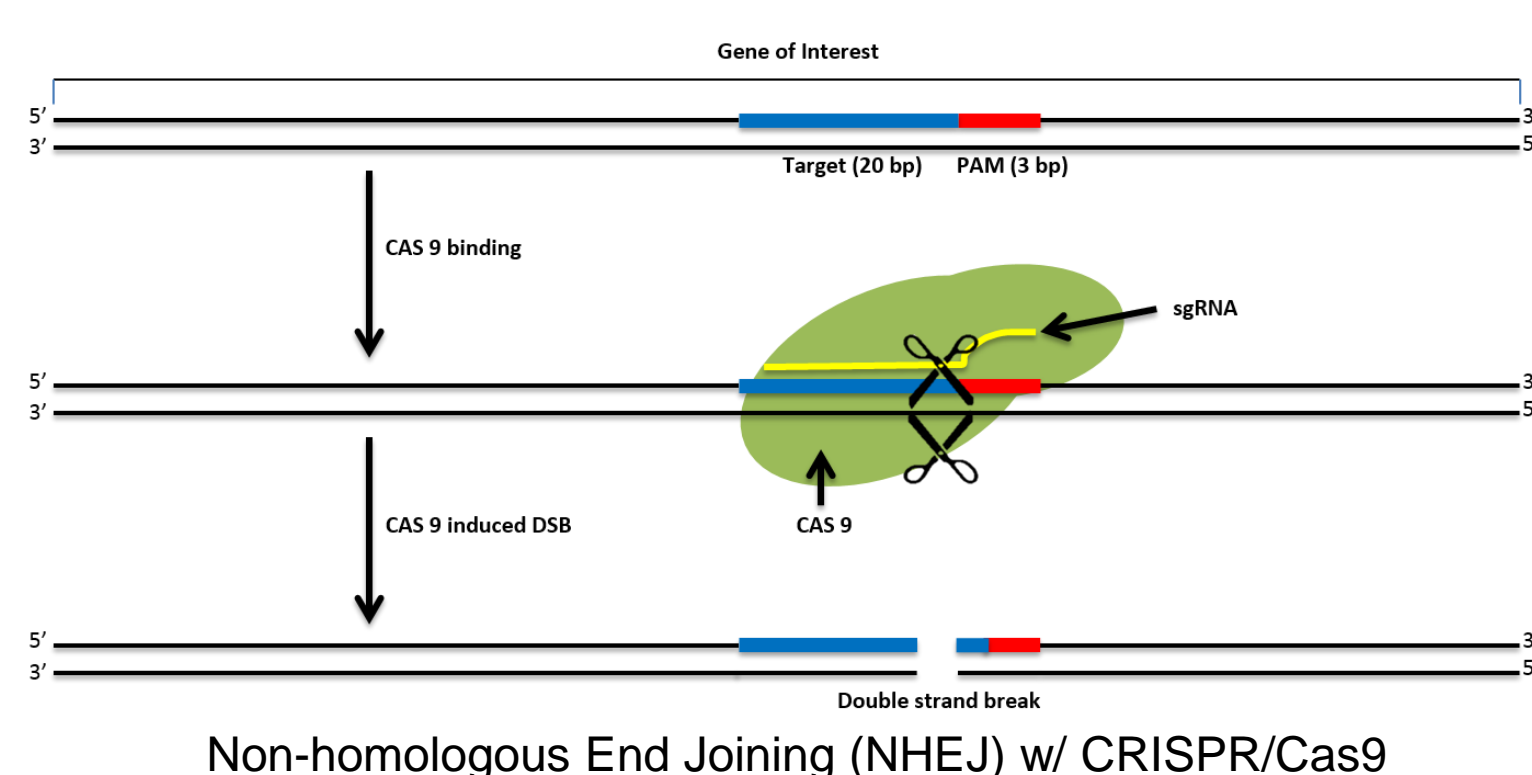
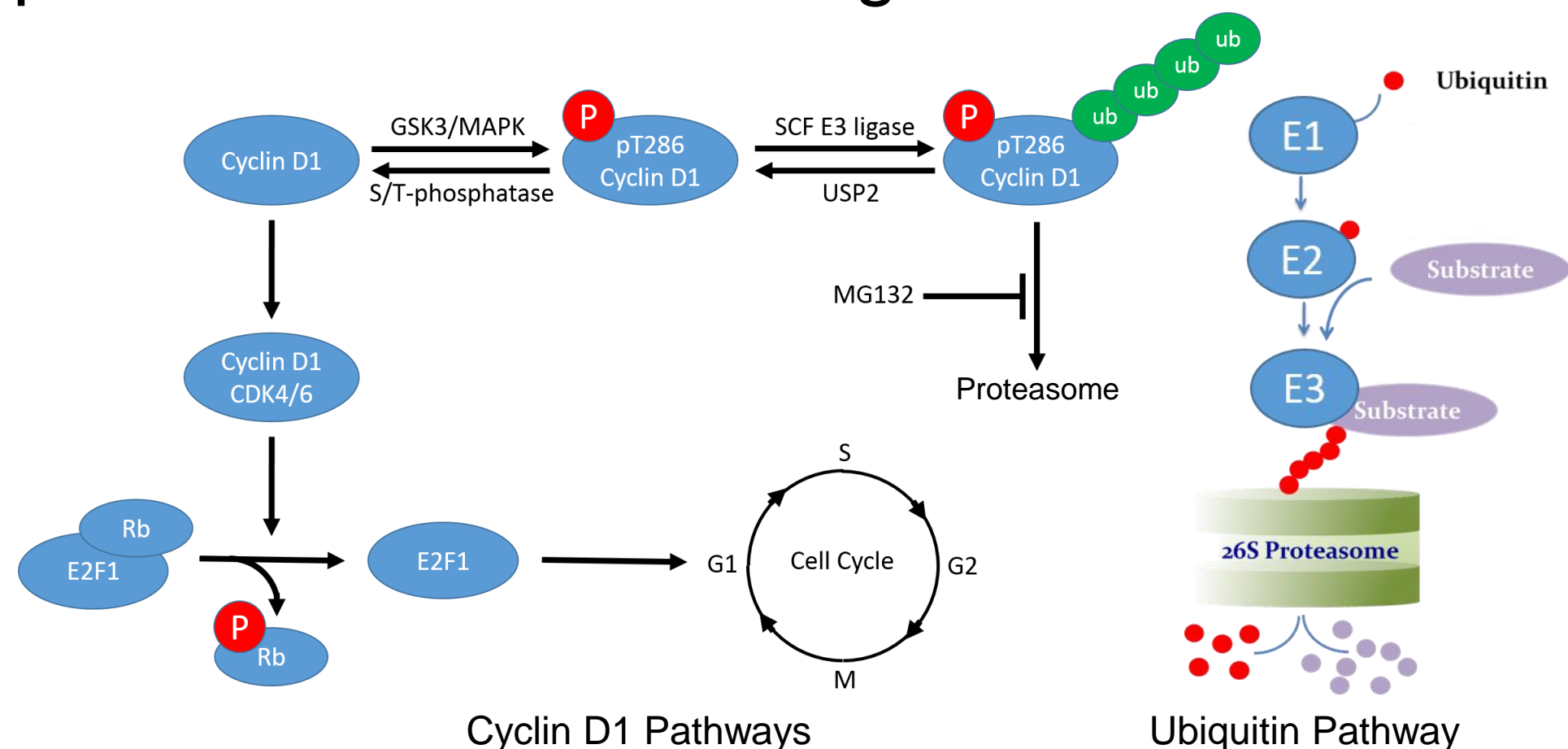


Regulation of cyclin D stability by the E3 ubiquitin ligase

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Overview

- CCND1 gene is frequently amplified or translocated in cancer cells, correlating to metastasis and shorter patient survival
- Mutated cyclin D inhibits phosphorylation of the degradation start site, increasing protein stability and transcription factor activation
- Radiotherapy was simulated by exposing human osteosarcoma cells with the protein mutations to ionizing and UV radiation
- Genome editing via CRISPR/Cas9 can be used to knock-out targeted genes and provide an insight into the pathways being utilized
- A potential correlation could be made between protein stabilities and degree of radiosensitivity



Impact

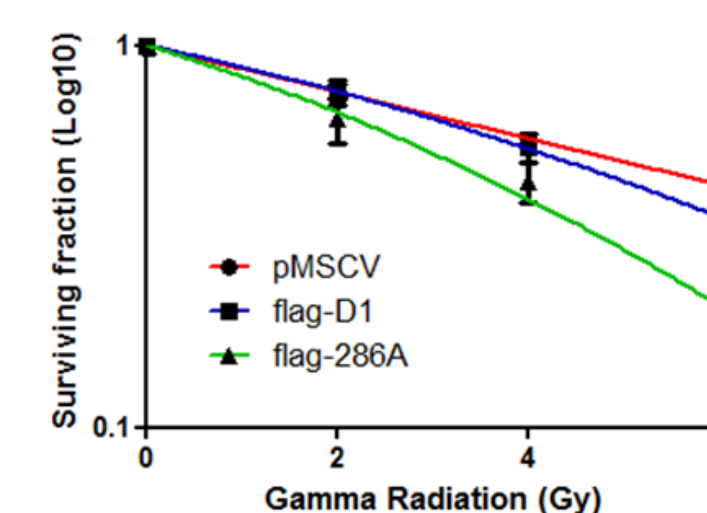
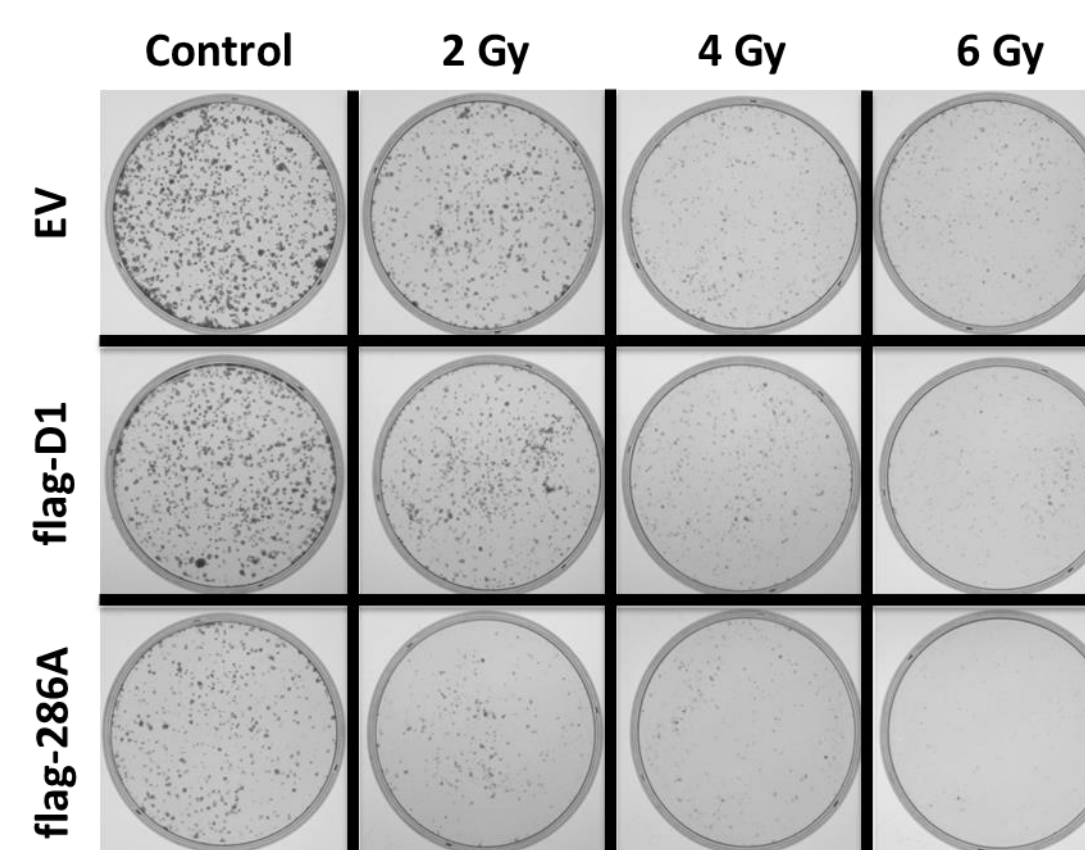
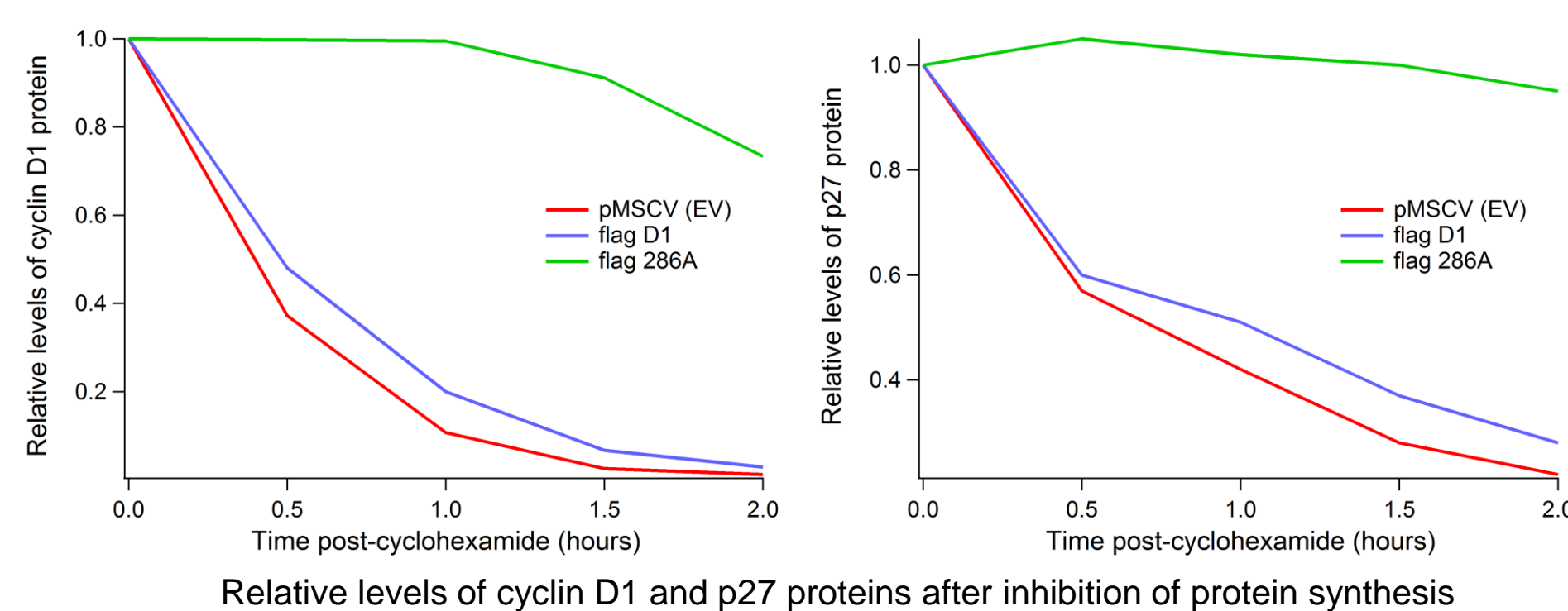
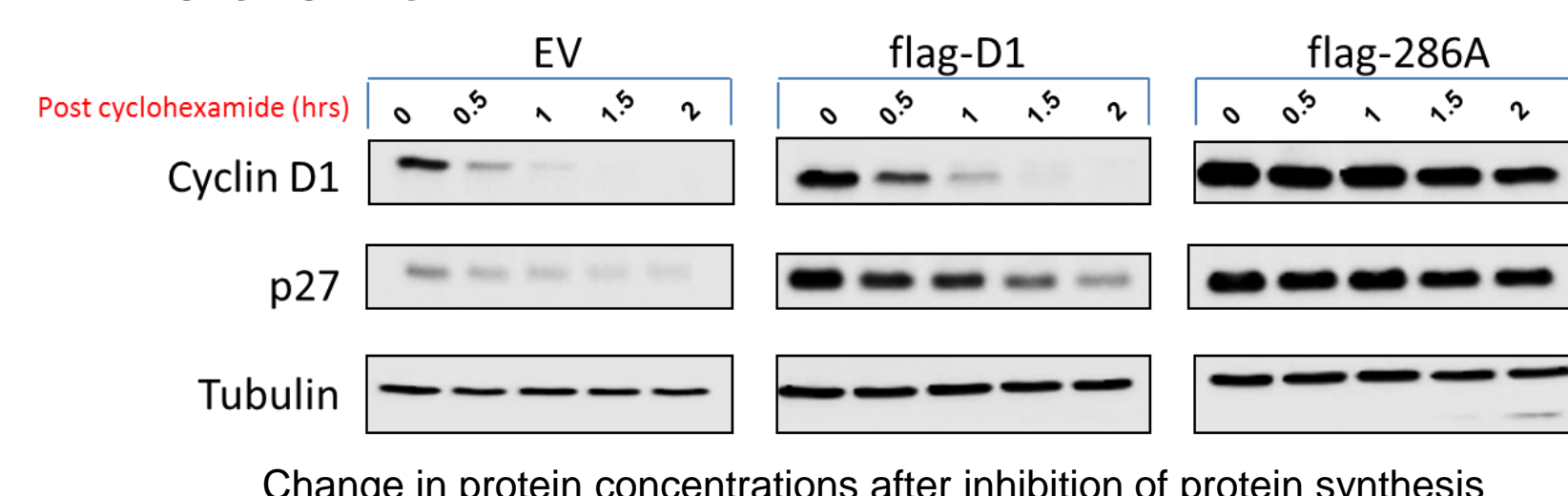
- If a correlation can be identified, therapies could be tailored for specific cancer types
- Determine the pathway by which radiosensitivity is initiated and identify the methods by which cancer cells react to DNA damage

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Key Findings

- Mutated cells showed:
 1. Increased stability for p27 and p21 tumor suppressor proteins
 2. Slower proliferation times
 3. Increased radiosensitivity when exposed to both ionizing and UV radiation



Radiosensitivity of cancer cells when exposed to varying doses of ionizing radiation

Explanation

- Cancers with CCND1 mutations may be better suited for radiotherapy treatment
- Re-testing cancer cells with the p27 and p21 coding genes knocked out will allow for better determination of the pathways responsible for radiosensitivity
- Slower proliferation times may be indicative of less aggressive cancers with longer recurrence periods