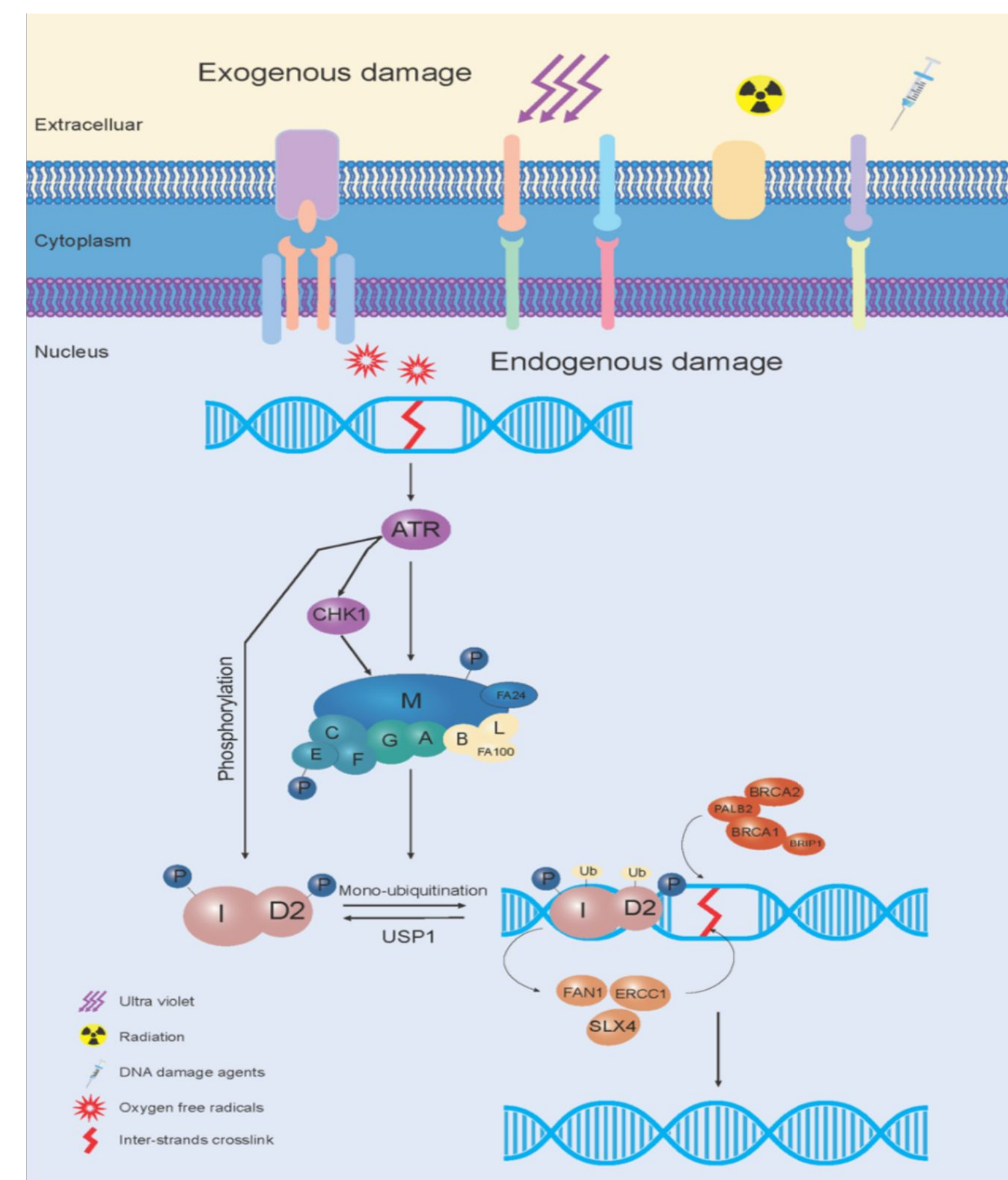


Background

Fanconi Anemia/BRCA Pathway

- Activates the DNA damage response (DDR) to double-stranded DNA breaks which allows for homologous recombination (error-free DNA repair)



Fang C-B et al (2020) *Front. Cell Dev. Biol.* 8:160.

Fanconi Anemia – Clinical Presentation

- Autosomal recessive disease related to biallelic mutations in numerous FA pathway proteins.¹⁻⁴
- Patients with FA exhibit bone marrow failure and a predisposition to developing cancers at a young age.^{4,5}
- Head and neck squamous cell carcinomas (HNSCC) are developed at a 706 observed/expected ratio.⁶

Immune Modulators in Fanconi Anemia

- IFN- γ is overexpressed in the bone marrow of Fanconi Anemia patients.⁸
- Cancer cells can survive IFN- γ cytotoxicity by expressing the programmed death 1 ligand (PD-L1)⁹
- The interaction between PD-L1 and programmed death 1 (PD-1) is also thought to decrease the T cell response¹⁰ by blocking T cell activation and even induces T cell apoptosis.¹¹

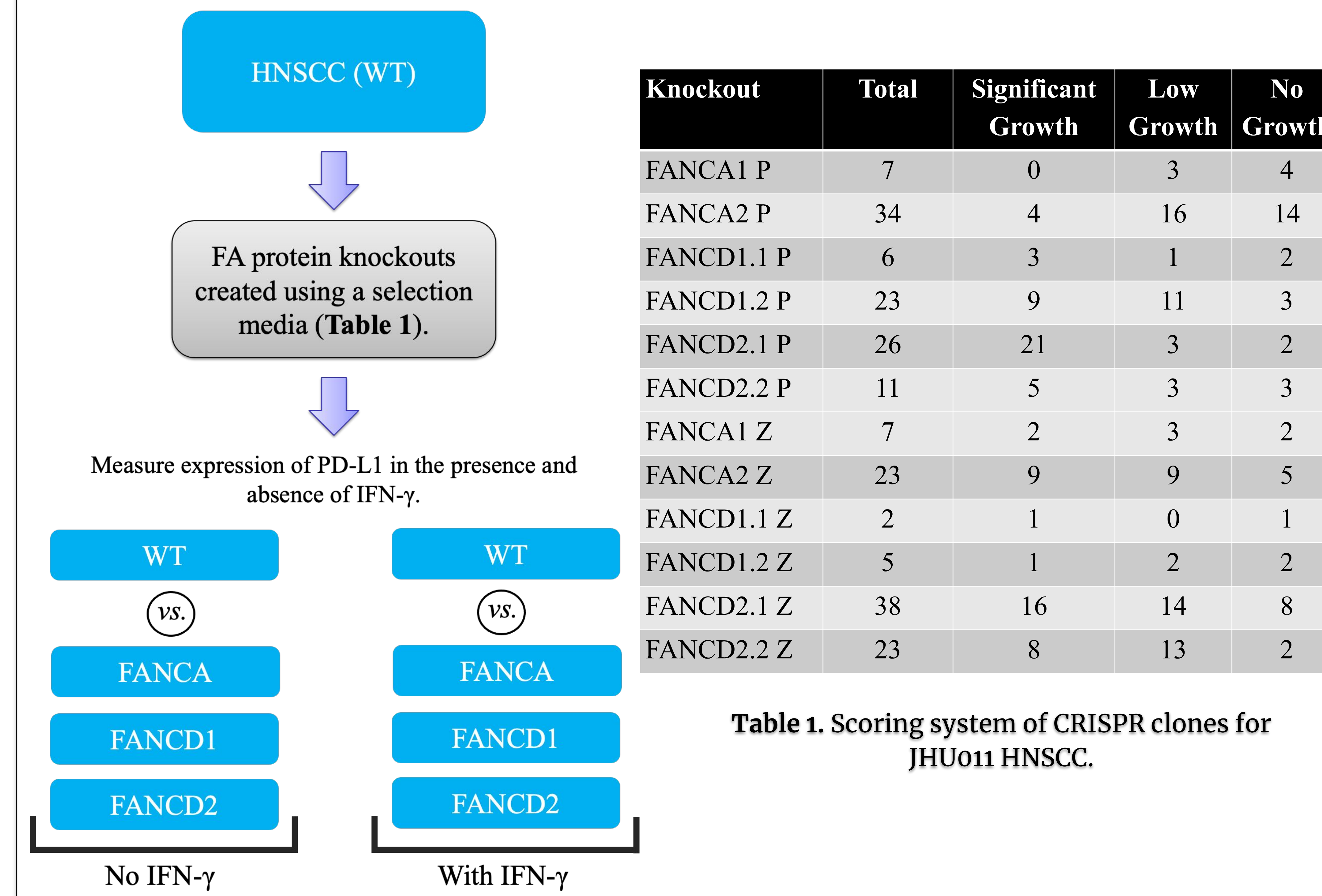
Goal

- To evaluate PD-L1 expression in both the presence and absence of IFN- γ in FA-mutated versus non-mutated HNSCC.

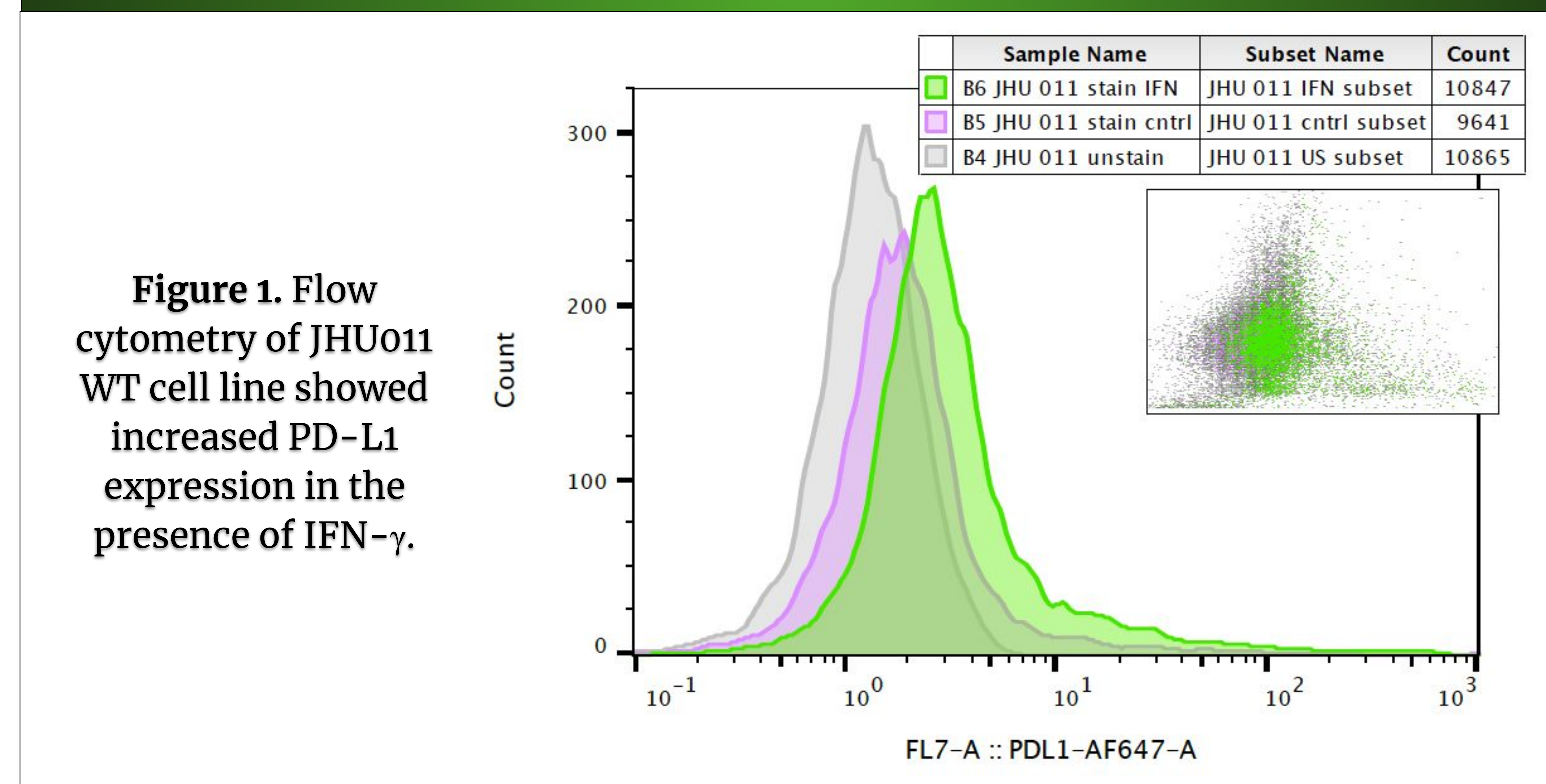
Hypothesis

- FA-mutated HNSCC will have higher levels of PD-L1 expression both in the presence and absence of IFN- γ compared to non-FA-mutated HNSCC. This may provide a rationale for using PD-1 checkpoint immunotherapy for these tumors.

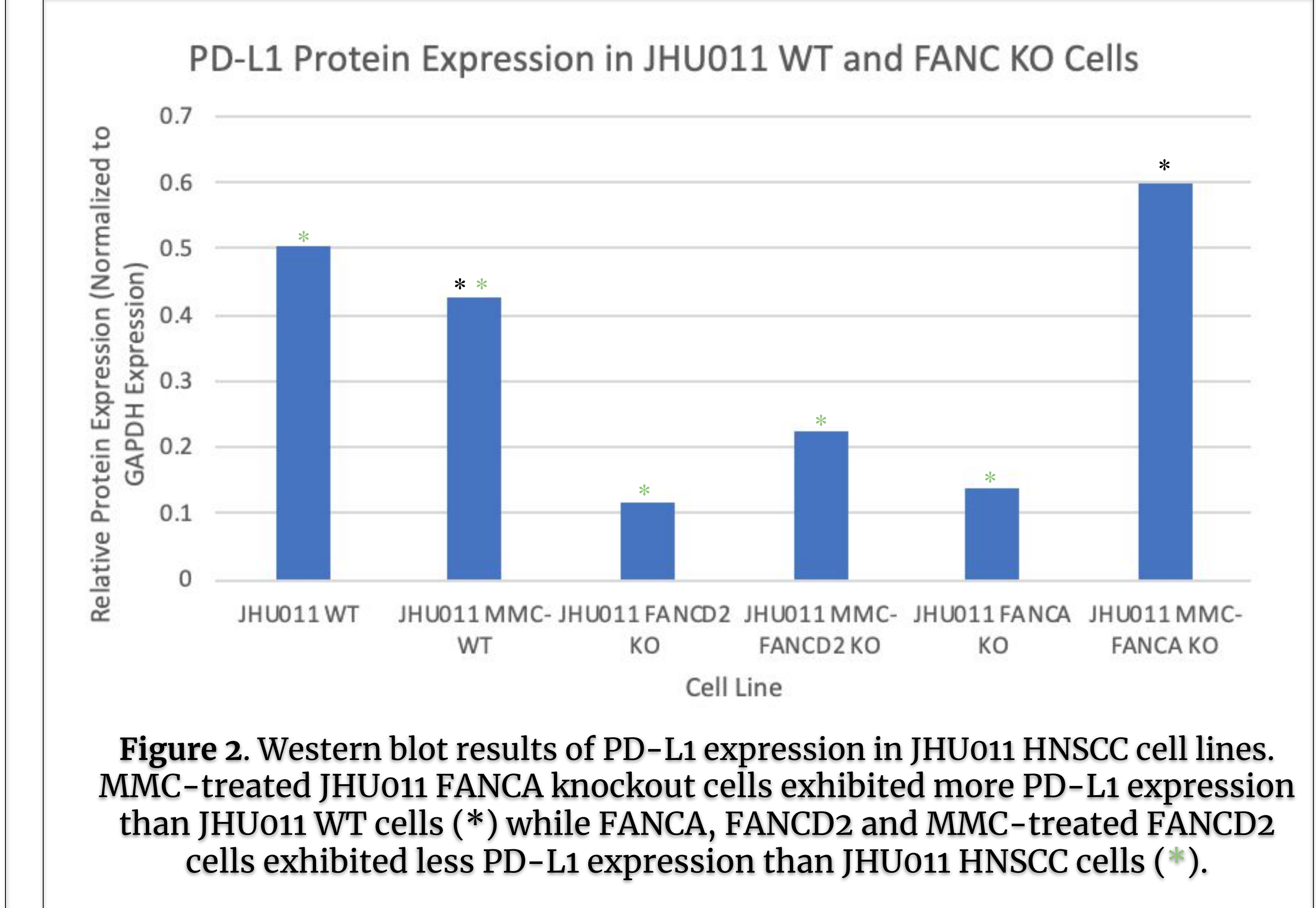
Methods



Results



Results Continued



Conclusions

- PD-L1 expression in HNSCC is increased in the presence of IFN- γ .
- PD-L1 expression is present in FA knockout HNSCC cells and is robustly increased in FANCA knockout cells treated with MMC.
- This data suggests that PD-L1 may be a target for checkpoint immunotherapy in HNSCC with FA mutations.

Future Directions

- Flow cytometry on JHU011 FA knockout cell lines to measure the response of PD-L1 expression to INF- γ .
- Create a humanized FA knockout HNSCC mouse model to measure response to PD-1 checkpoint immunotherapy.

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