

# Plinabulin, a microtubule destabilizing agent, improves tumor control by enhancing dendritic cell maturation and CD8 T cell infiltration in combination with immunoradiotherapy

Shinya Neri<sup>1</sup>, Amrish Sharma<sup>1</sup>, G. Kenneth Lloyd<sup>2</sup>, Ramon Mohanlal<sup>2</sup>, James R. Tonra<sup>2</sup>, Lan Huang<sup>2</sup>, Steven H. Lin<sup>1</sup>

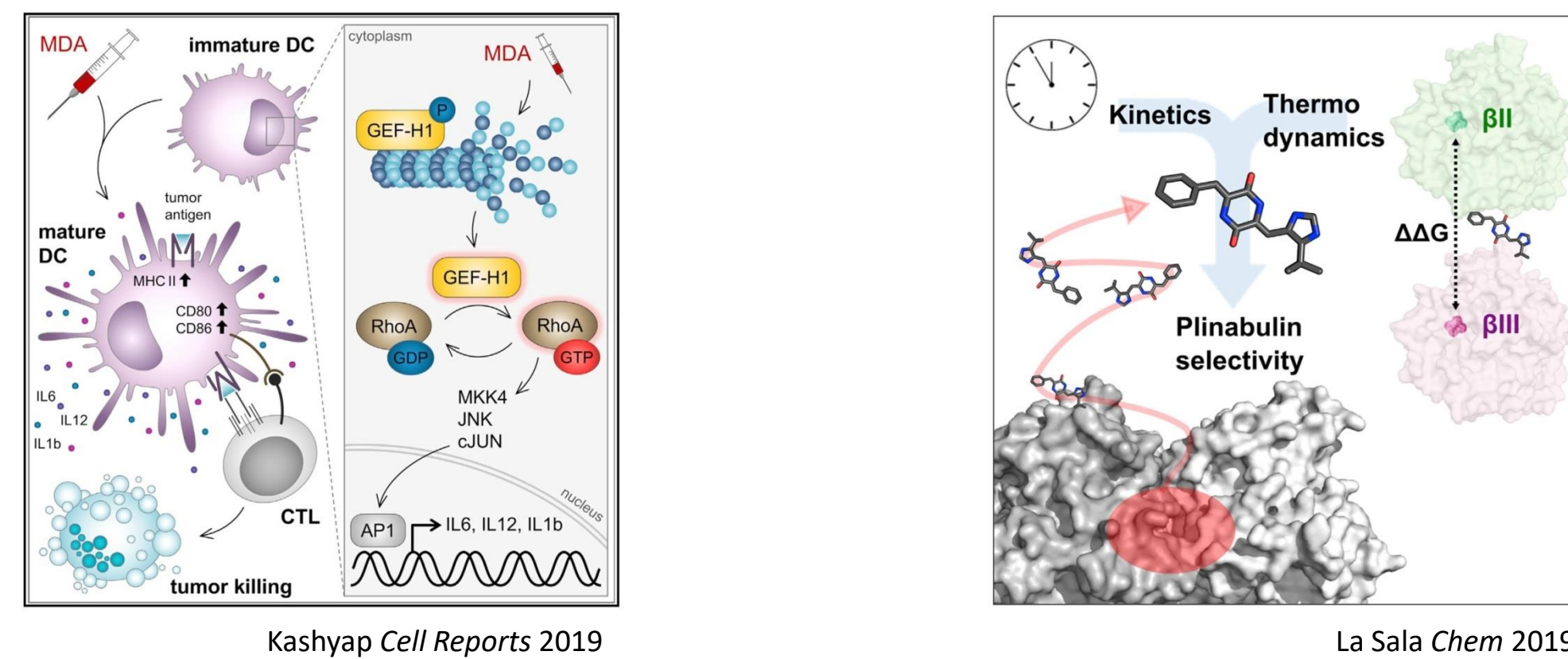
<sup>1</sup>Department of Experimental Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, <sup>2</sup>BeyondSpring Pharmaceuticals, Inc., New York, NY

## Introduction

### Maturation of dendritic cells (DCs)

- improving the effectiveness of immunoradiotherapy
- promoted by microtubule destabilizing agents

### Plinabulin as a candidate DC activator



## Material & Method

### Dendritic cell lines:

SP37A3 and XS106 cells from BALB/c and A/J mice, respectively

### Triple combination therapy *in vivo*:

TSA, mammary cancer cells from BALB/c mice

Female, 7-9 weeks of age, BALB/c mice

Anti-mouse PD-1 mAb (clone RMP1-14, 10mg/kg)

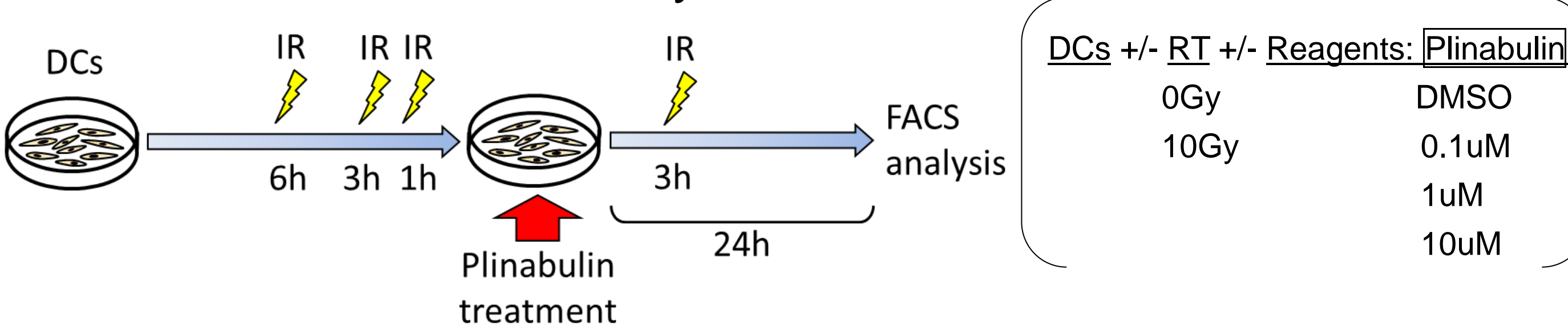
### Statistical analysis: Dunnett's test

(\* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$  versus control)

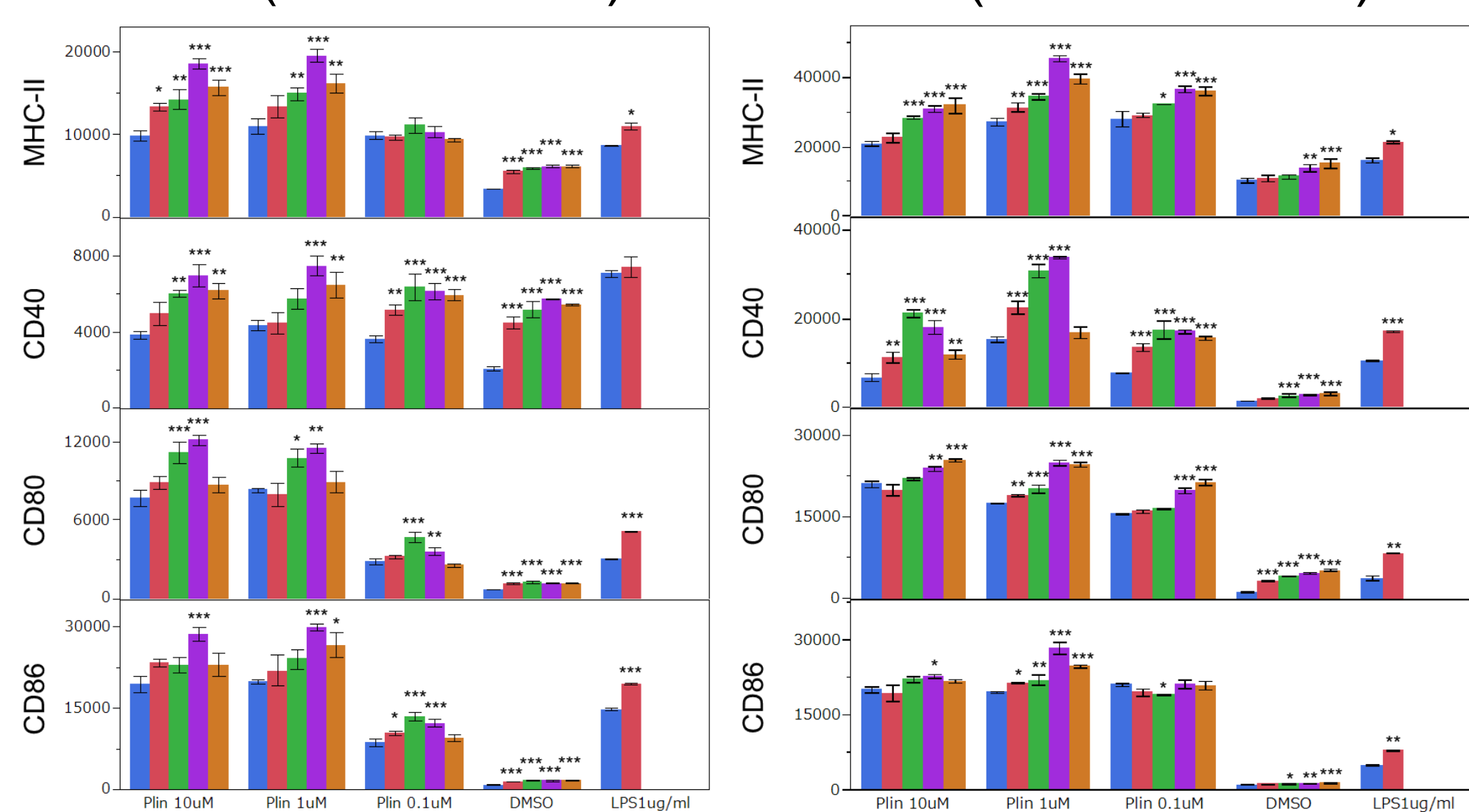
## Results 1

### Sequence of irradiation and Plinabulin therapy on DCs (Plinabulin or irradiation first?)

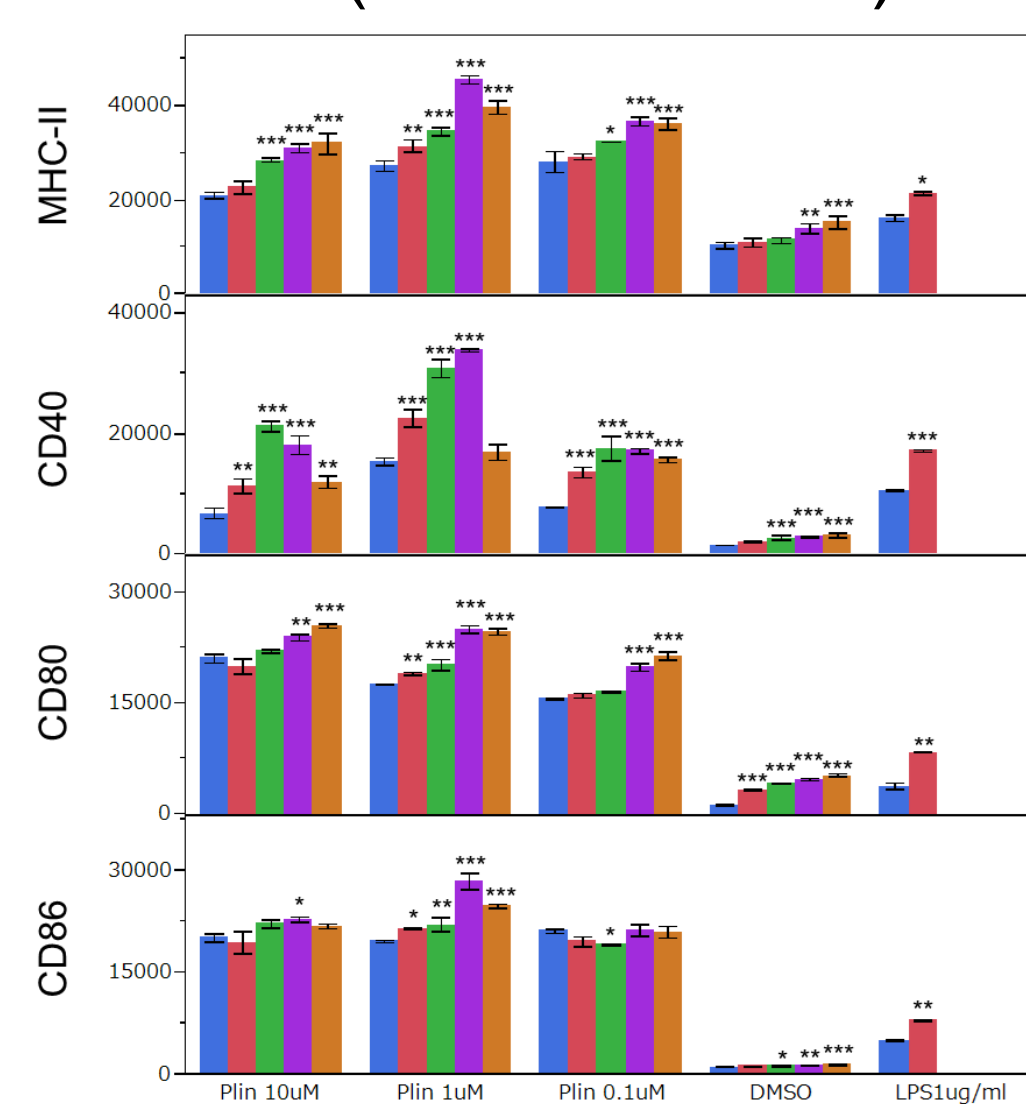
#### *In vitro* DC maturation assay



#### MFI (XS106 DCs)



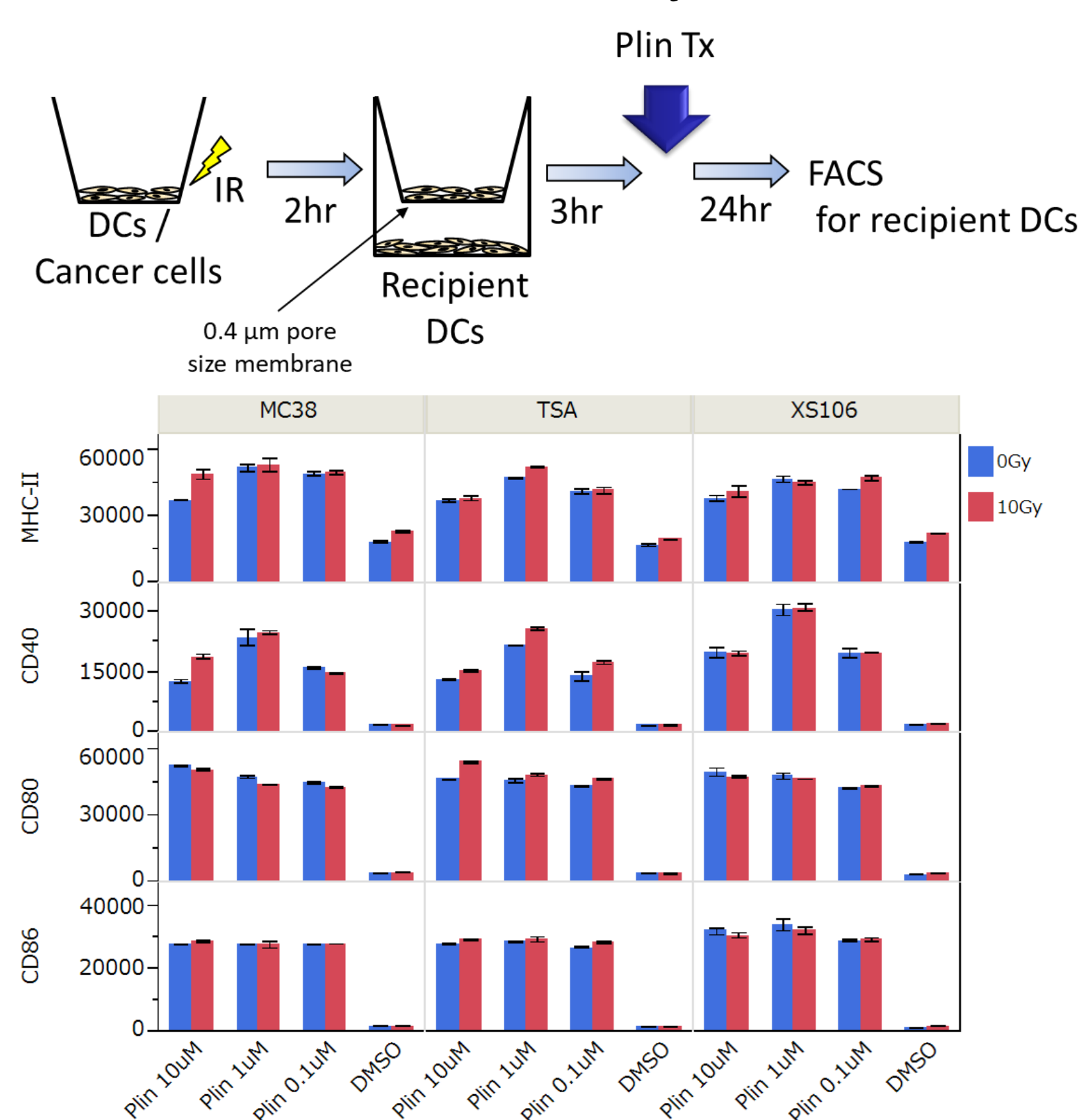
#### MFI (SP37A3 DCs)



Plinabulin Tx after IR upregulated DC maturation markers

## Results 2

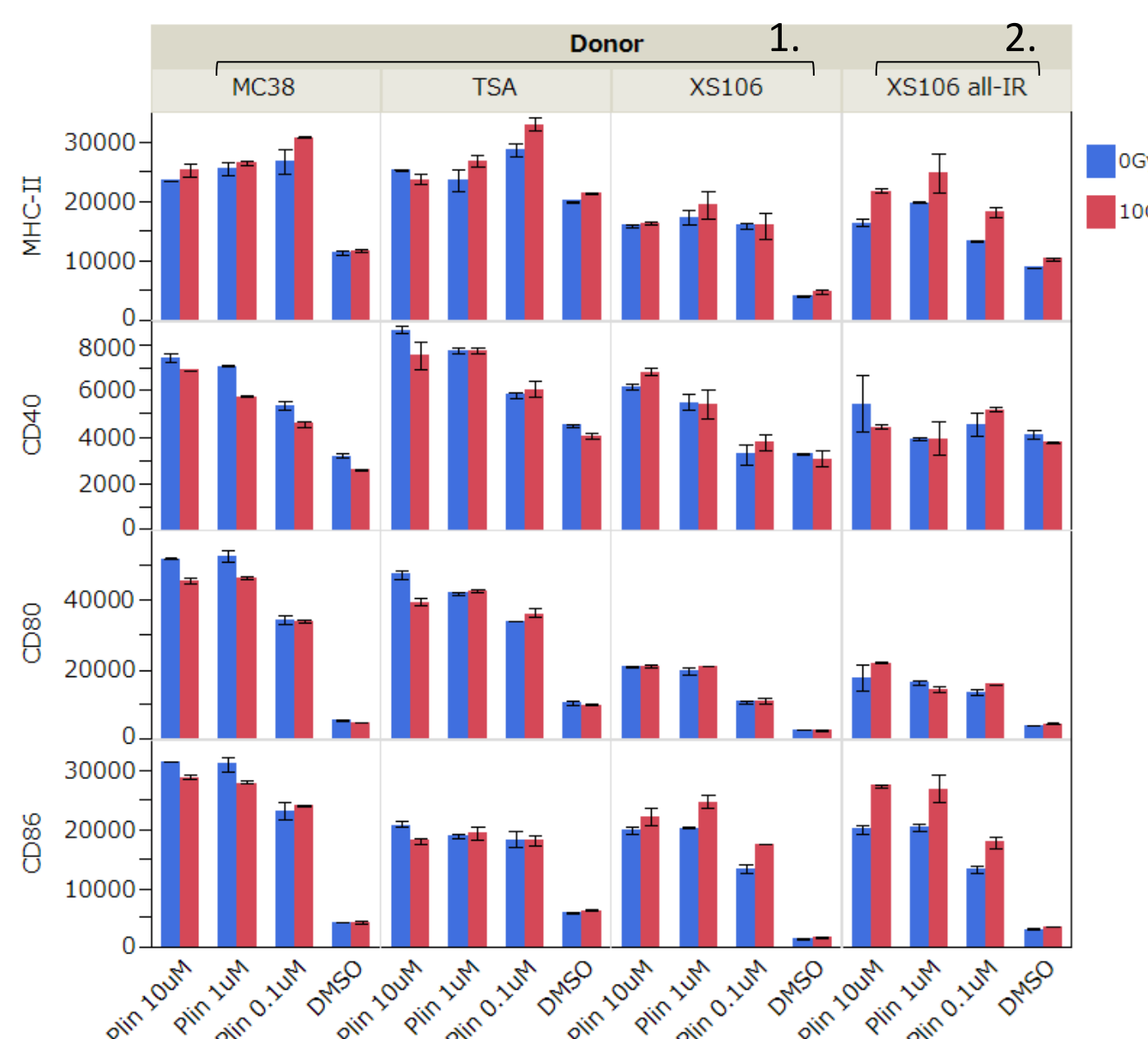
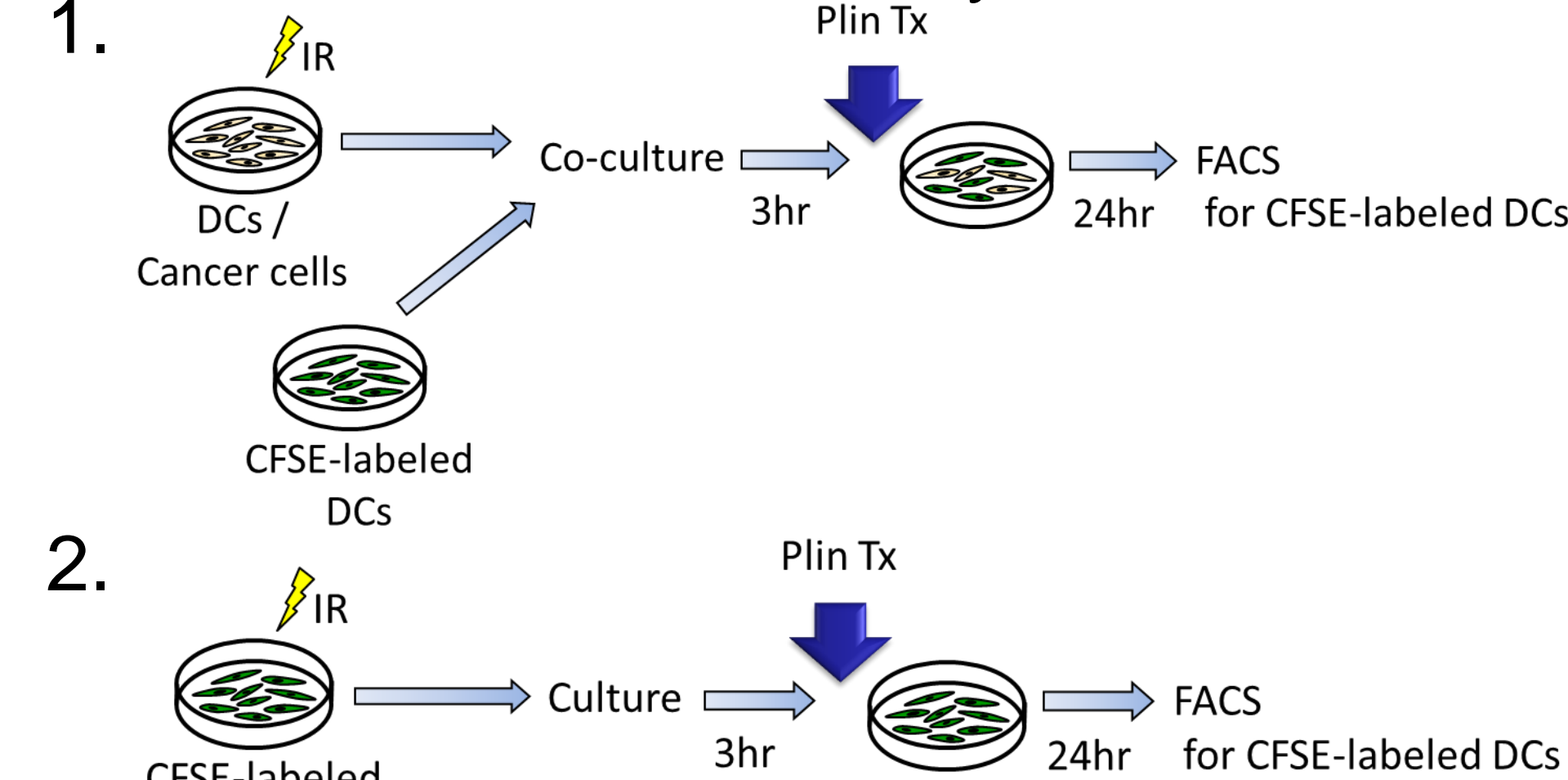
### Indirect DC maturation assay



Irradiated cells did not induce DC maturation indirectly

## Results 3

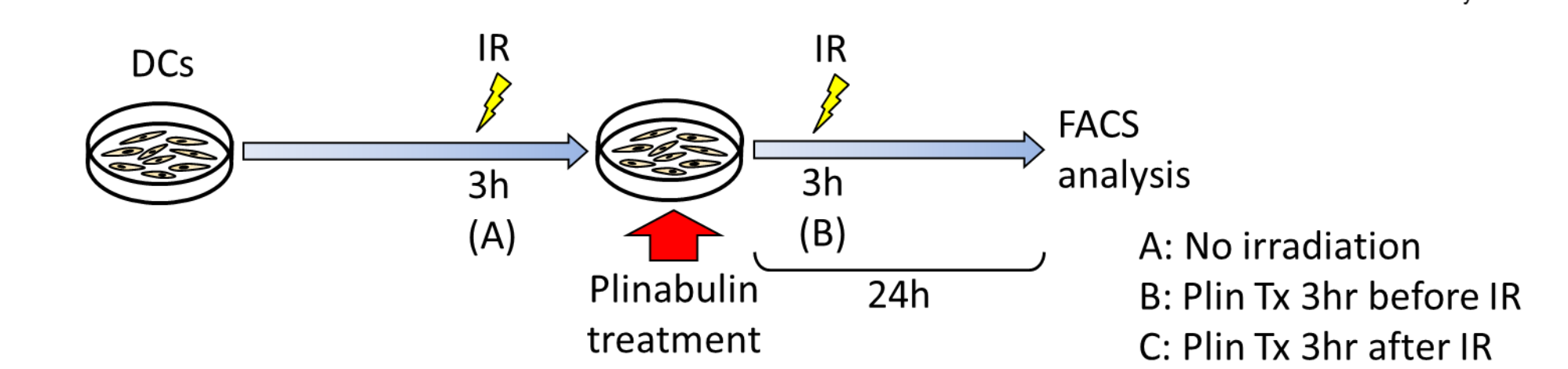
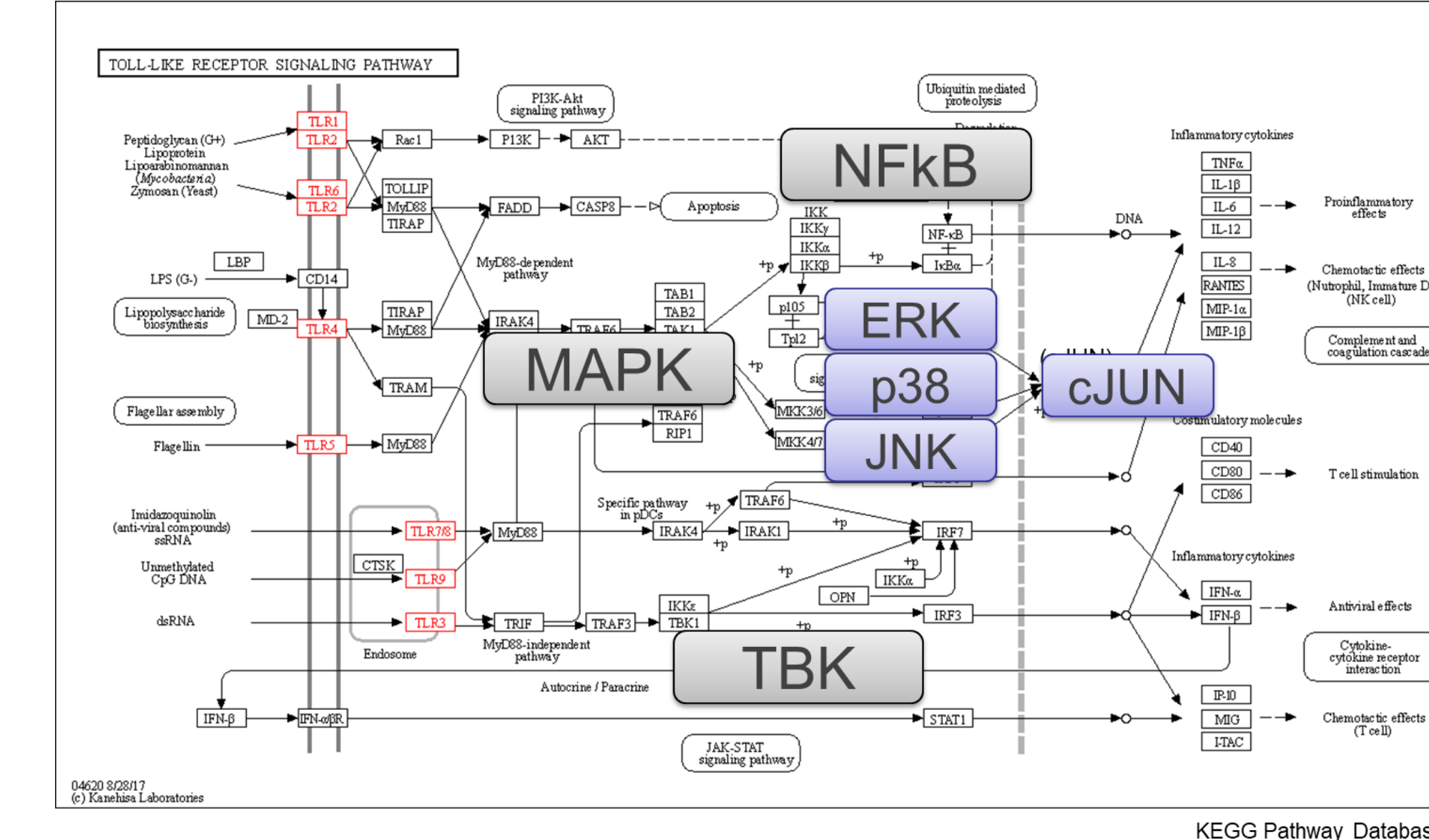
### Direct DC maturation assay



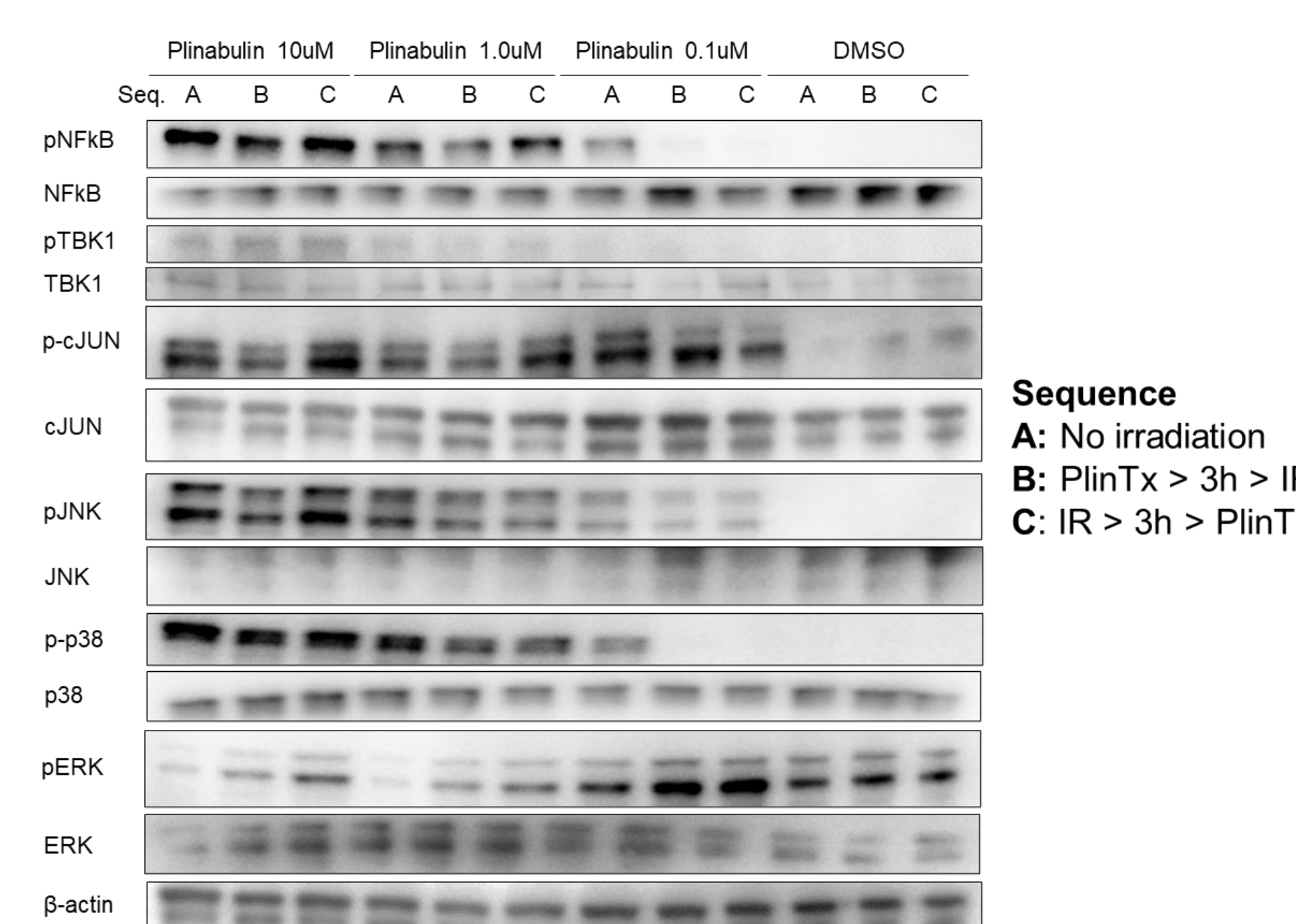
IR + PlinTx to DCs induced DC maturation directly

## Results 4

### Toll-Like Receptor Pathways



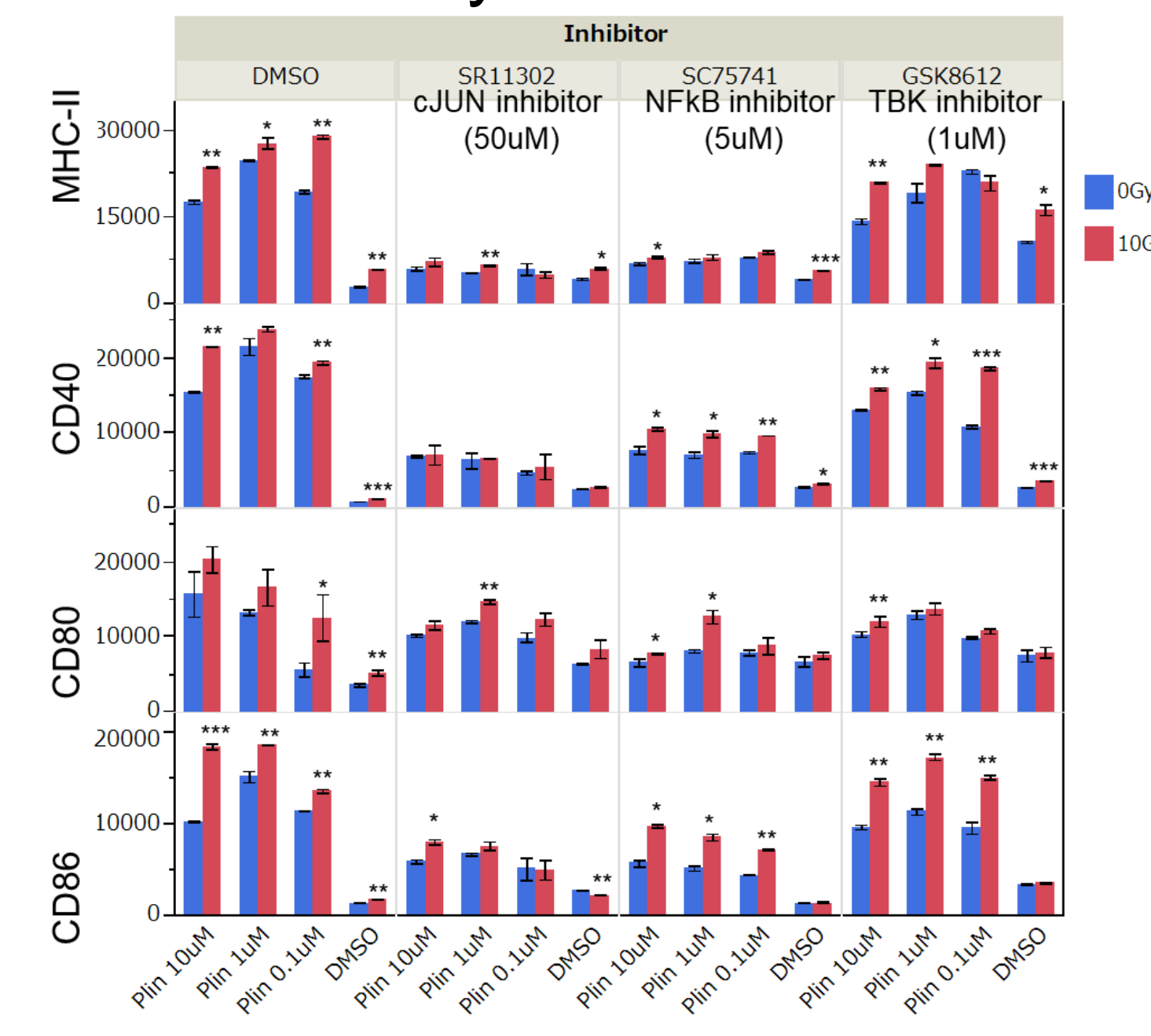
### XS106 DCs



Plinabulin Tx after IR upregulated phosphorylation of NFkB and cJUN

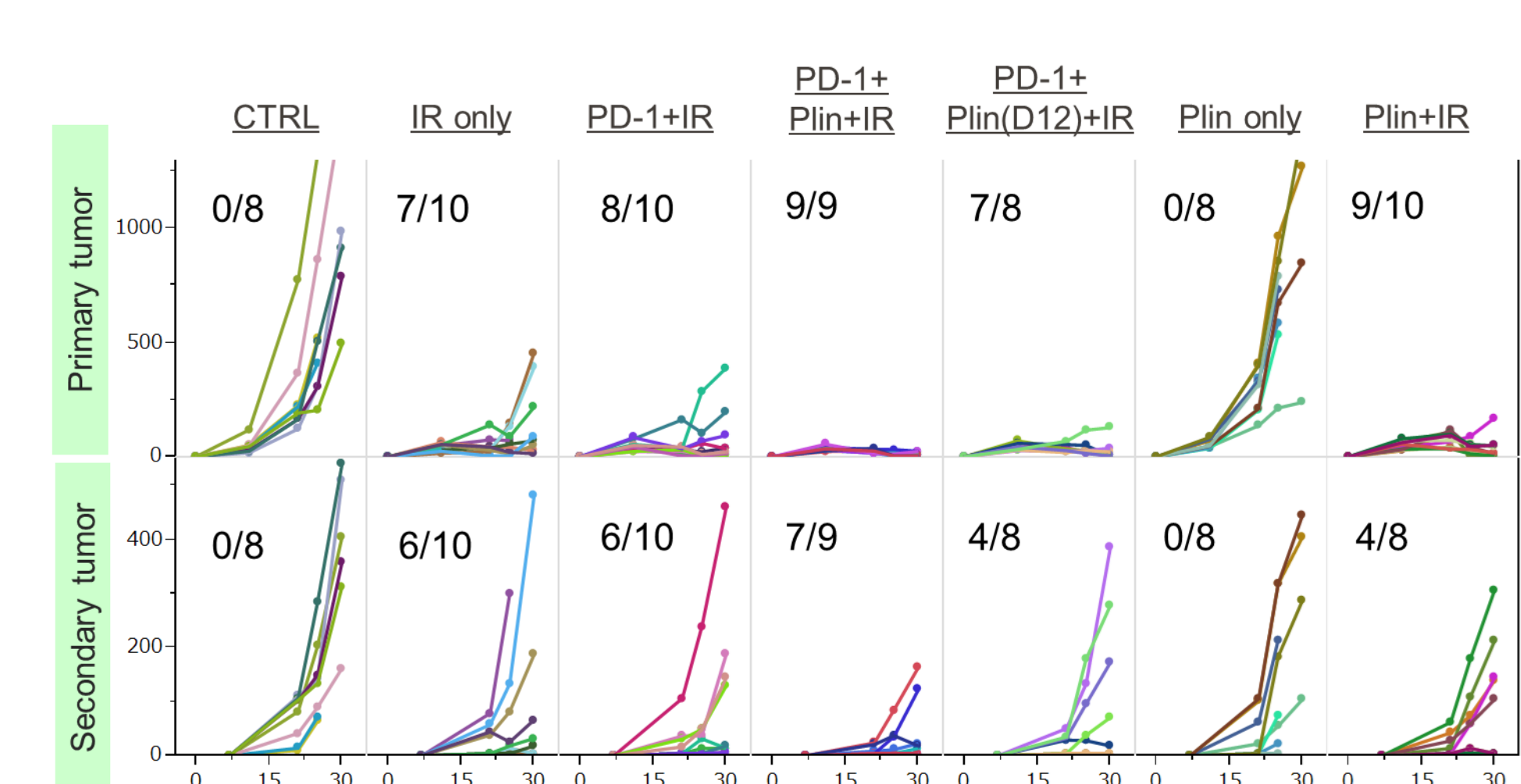
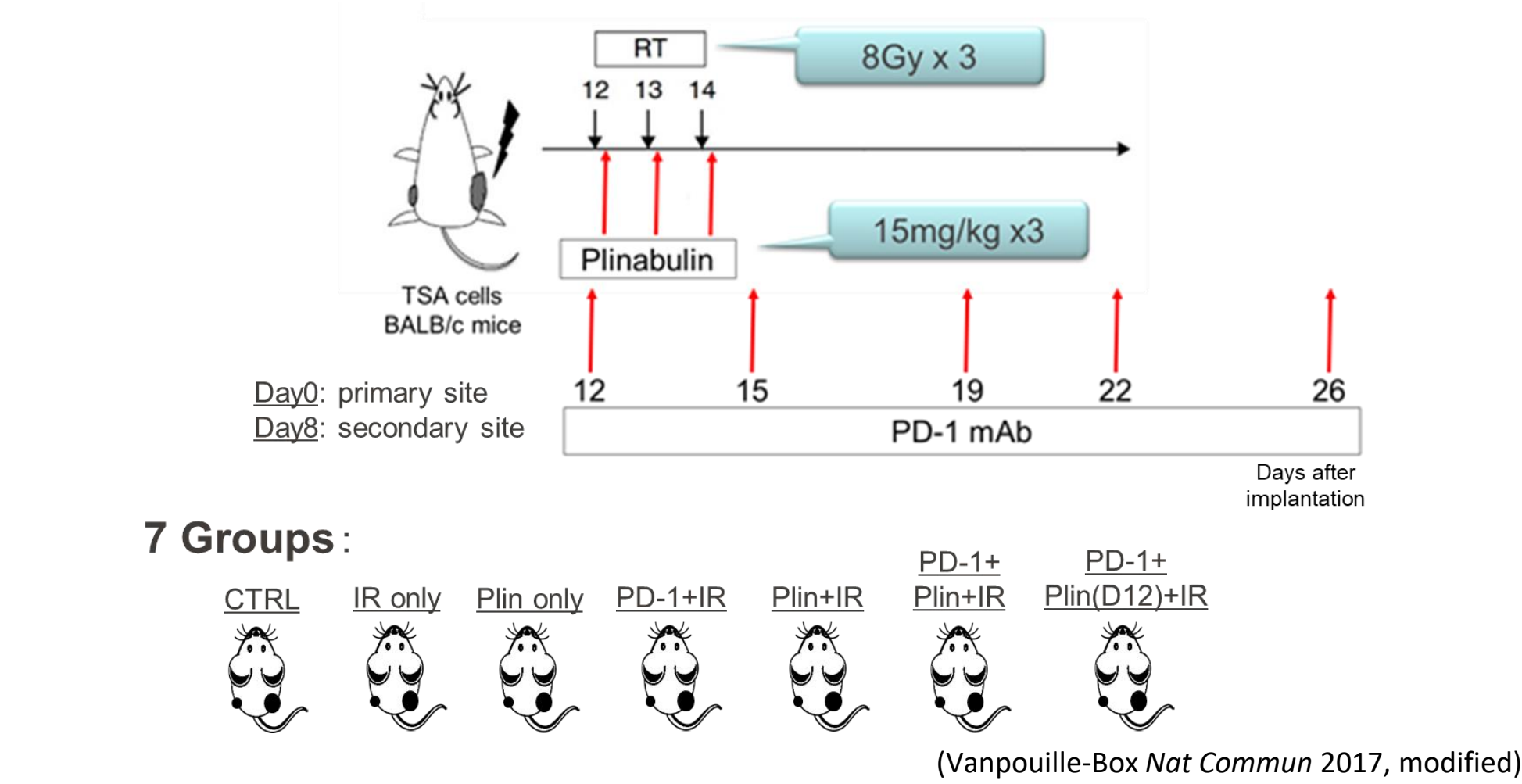
Plinabulin Tx after IR upregulated phosphorylation of JNK and ERK

### Inhibition assay

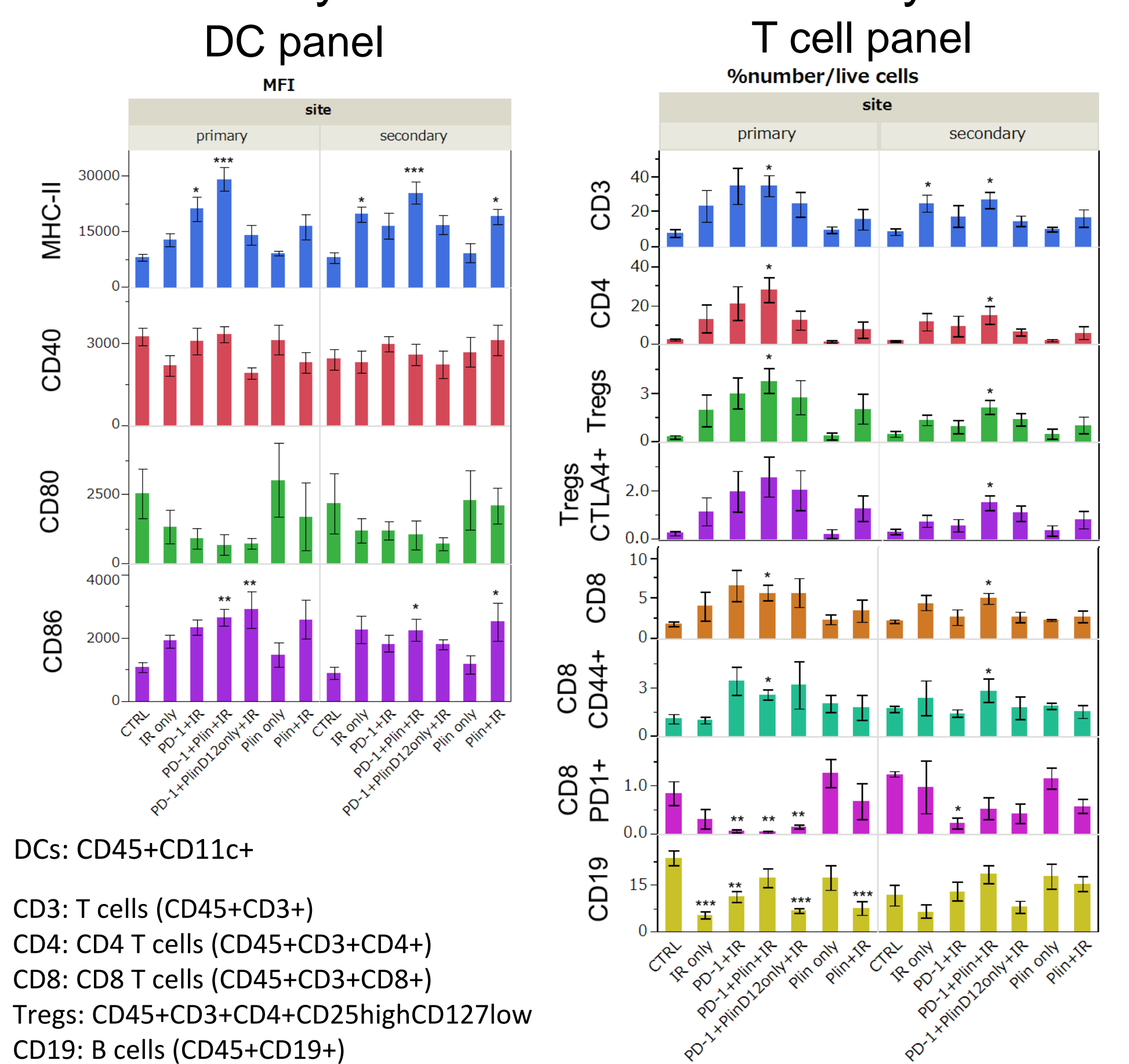


DC maturation due to IR + PlinTx is dependent on MAPK and NFkB pathways

## Results 5



### FACS analysis from tumors on Day 30



Triple therapy was effective and induced MHC-II expression on DCs and T cell filtration

## Conclusions

- In *in vitro* models, IR -> Plin was significantly an effective sequence in DC maturation. DC maturation is dependent on NFkB and MAPK pathways.
- In *in vivo* models, Triple therapy was effective and induced MHC-II expression on DCs and T cell filtration.