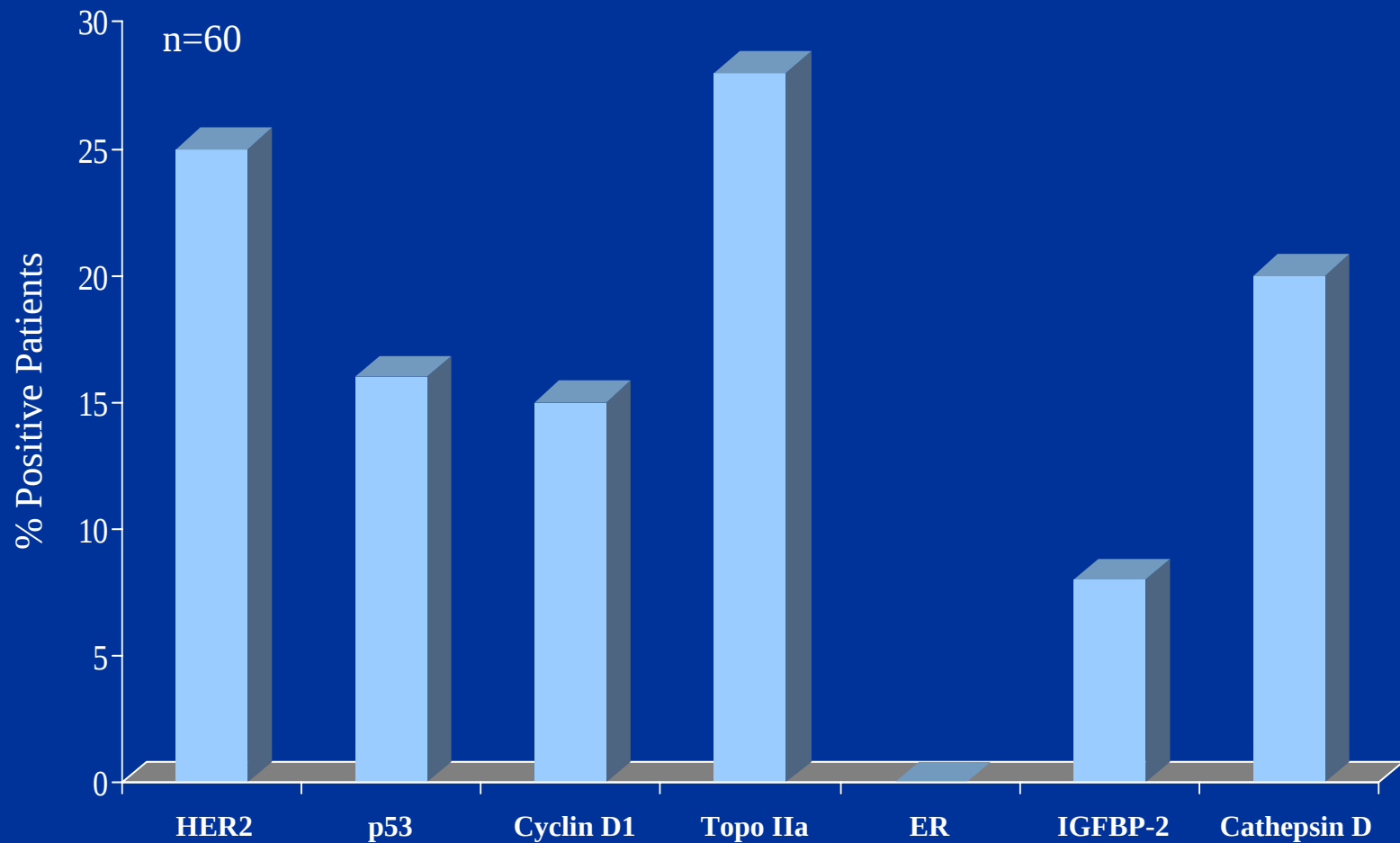


CD8 T cell-mediated Antitumor Effect of Imiquimod in a Mouse Model of Breast Cancer

Hailing Lu

Tumor Vaccine Group
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Seattle, WA

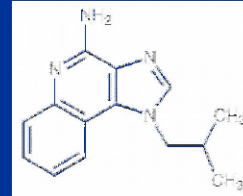
Incidence of Immunity in Breast Cancer



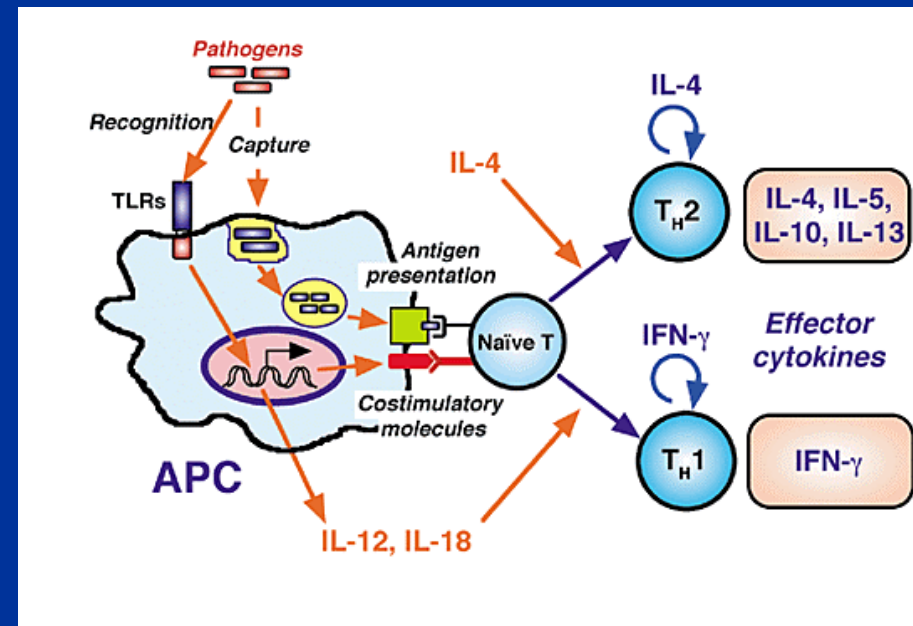
Breast Cancer Antigens

Goodell et al, 2005

TLR Activation - “the Danger Signal”



- Imiquimod: binds TLR7
- Activates innate and adaptive immune response
- Anti-viral and anti-tumor effect



Akira et al, Nat. Immunol, 2001

Chest Wall Recurrence in Breast Cancer



Kolodziejski L et al, Breast J, 2005

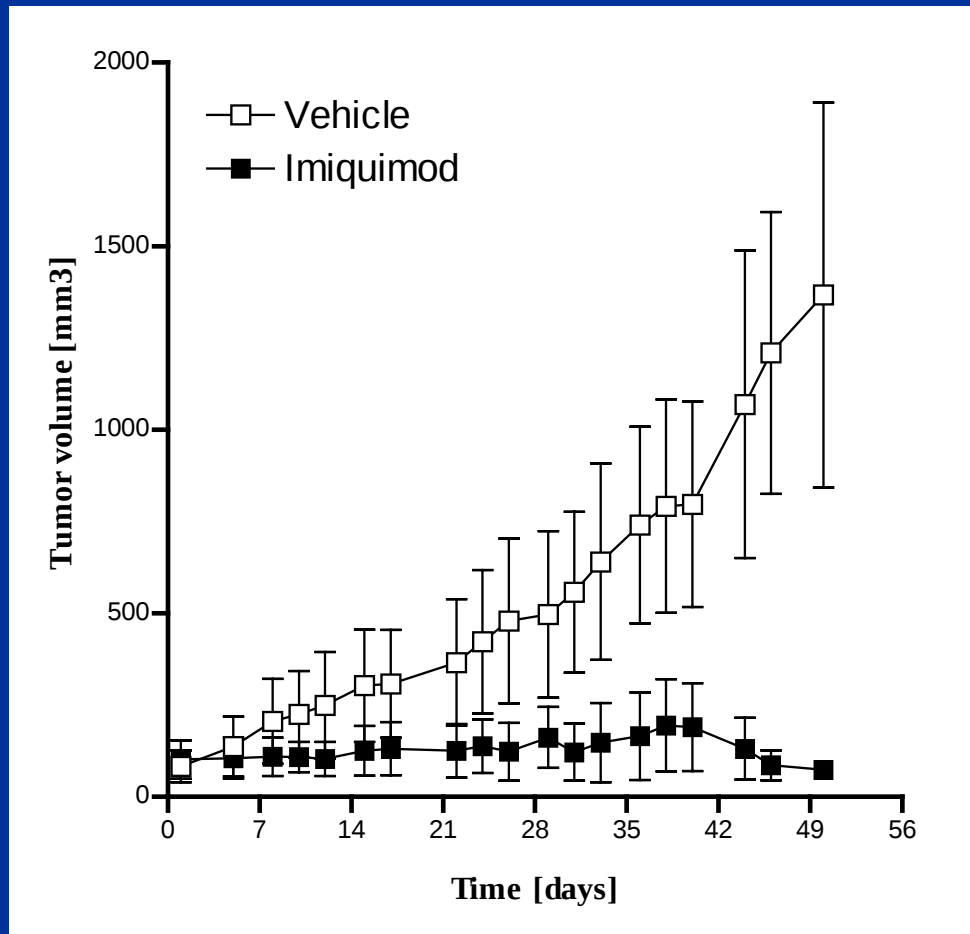
Can we use imiquimod?

Animal model of breast cancer

- neu-tg mice [FVB/N-TgN (MMTVneu)-202Mul]
- 70% of mice develop HER2+ tumor at 7-10 months of age
- Imiquimod or vehicle treatment started at palpable tumor

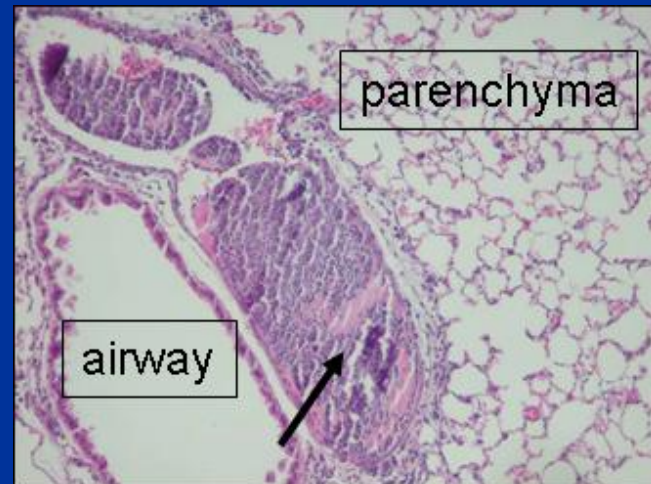


Topical Imiquimod Inhibits Tumor Growth

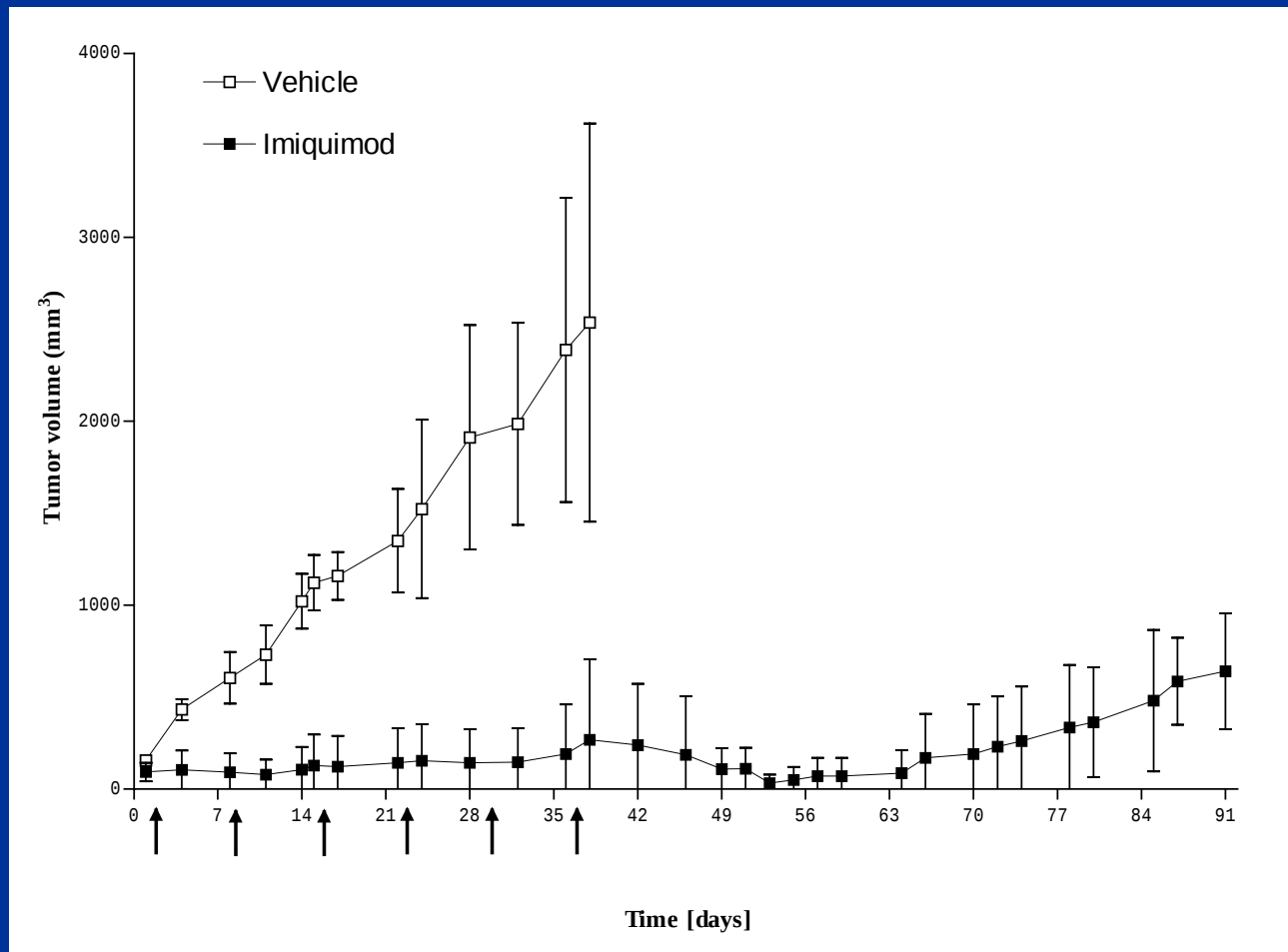


Imiquimod Inhibits Development of Metastasis

	Imiquimod	Vehicle
Multilobed tumor	2/11	8/10
Lung metastases	0/11	3/10



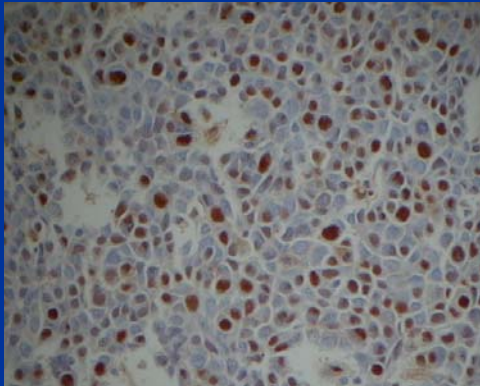
The Tumor Inhibitory Effect of Imiquimod Persists After Treatment Withdrawal



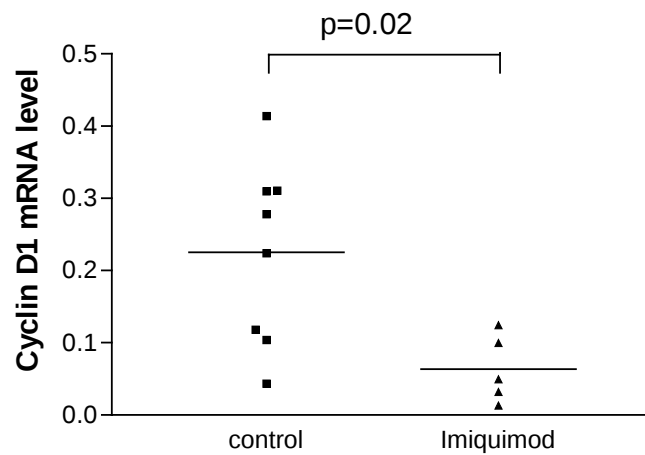
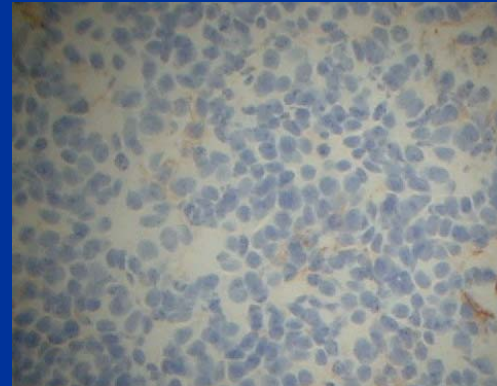
Imiquimod Inhibits the Proliferation of Tumor Cells

PCNA
staining

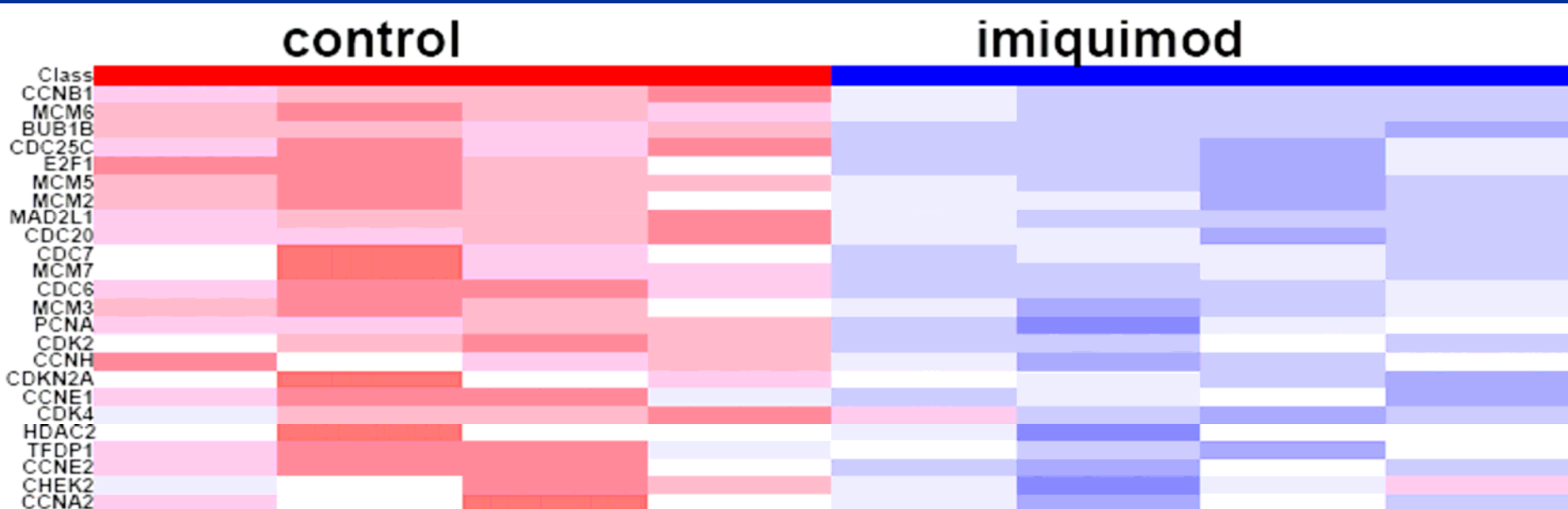
control



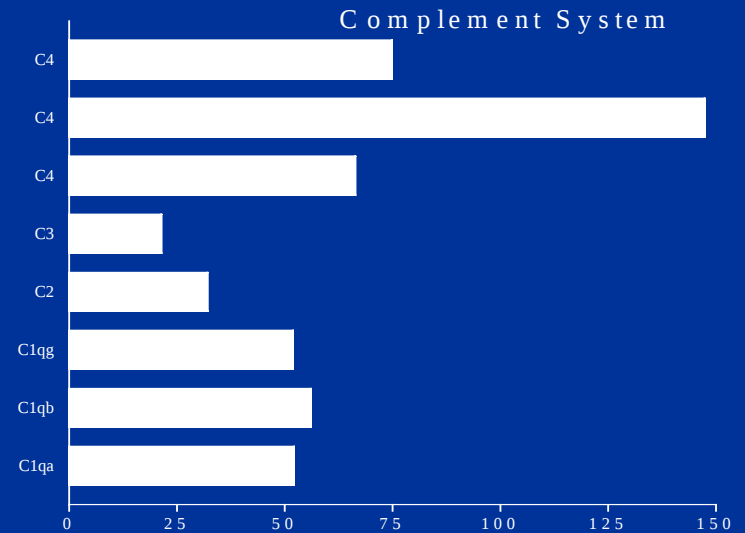
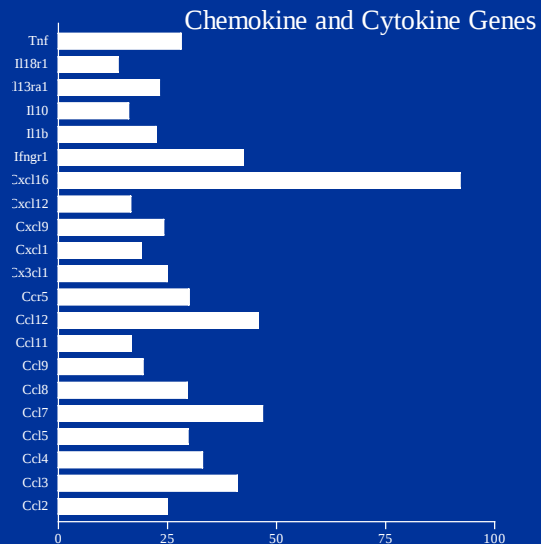
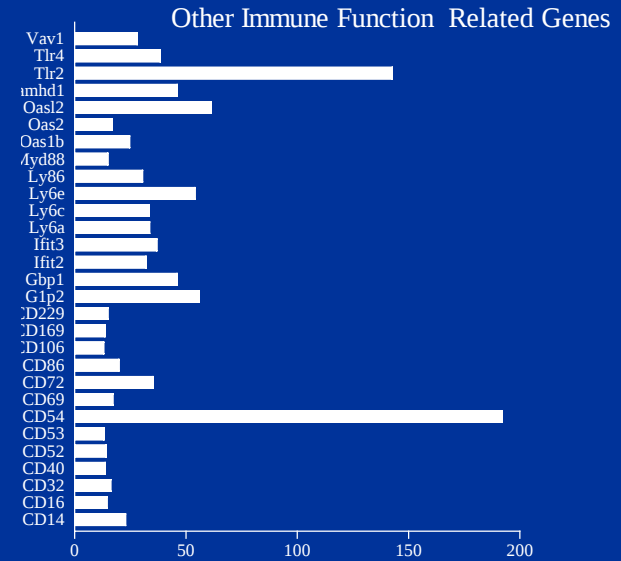
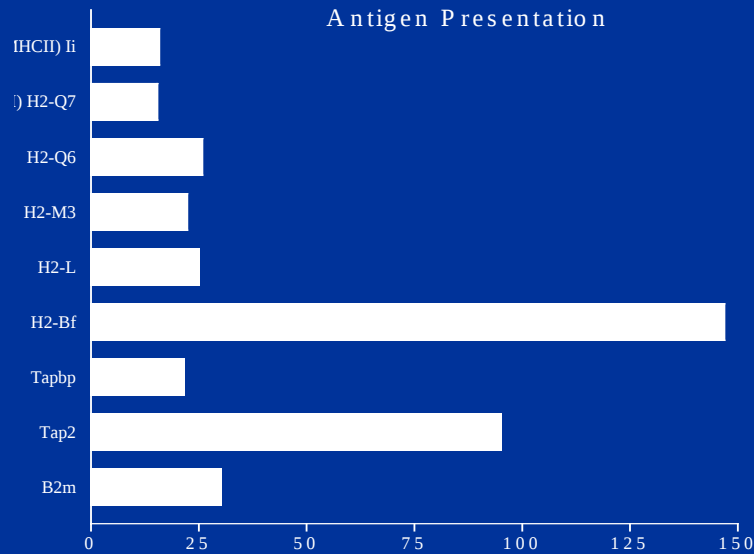
Imiquimod



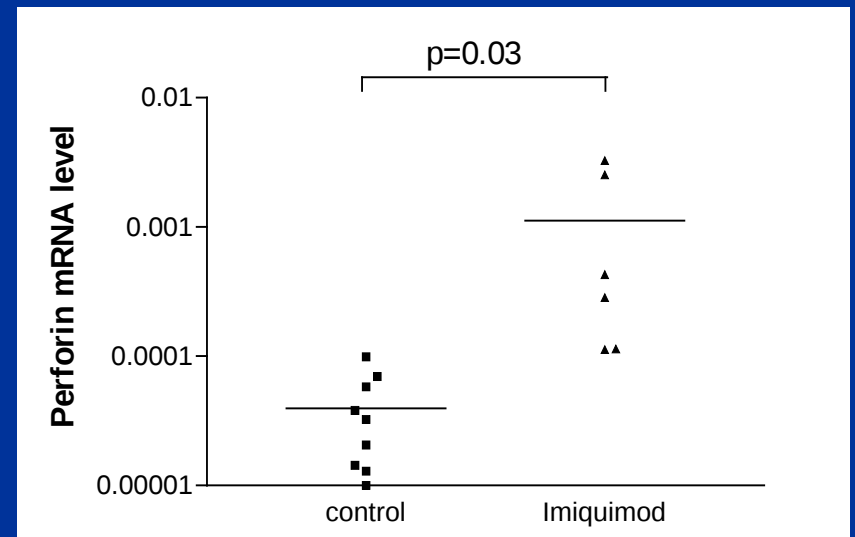
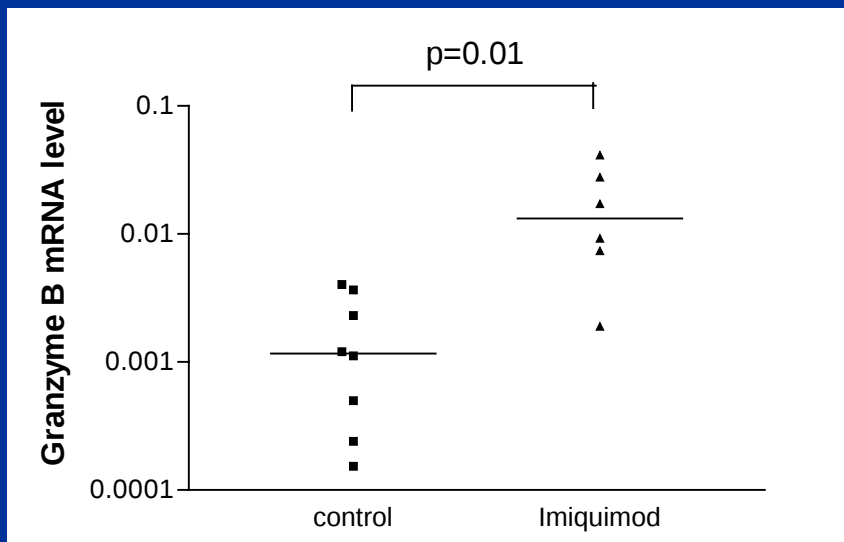
Down-regulation of Cell Cycle-related Genes after Imiquimod Treatment



Genes Up-regulated by Imiquimod



Imiquimod Induces Expression of Immune Effector Molecules



Summary

- Topical Imiquimod stops the growth of spontaneous mammary tumors in neu-tg mice
- Imiquimod inhibits lung metastasis and the tumor inhibitory effect persists after treatment withdrawal
- Imiquimod changes the tumor microenvironment by up-regulating the expression of MHC I on tumor cells and recruiting CD8 T cells.
- The tumor inhibitory effect of imiquimod is dependent on CD8 T cells.

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