

FoxP3 expression in tumour cells, virally transformed B cells and other cells

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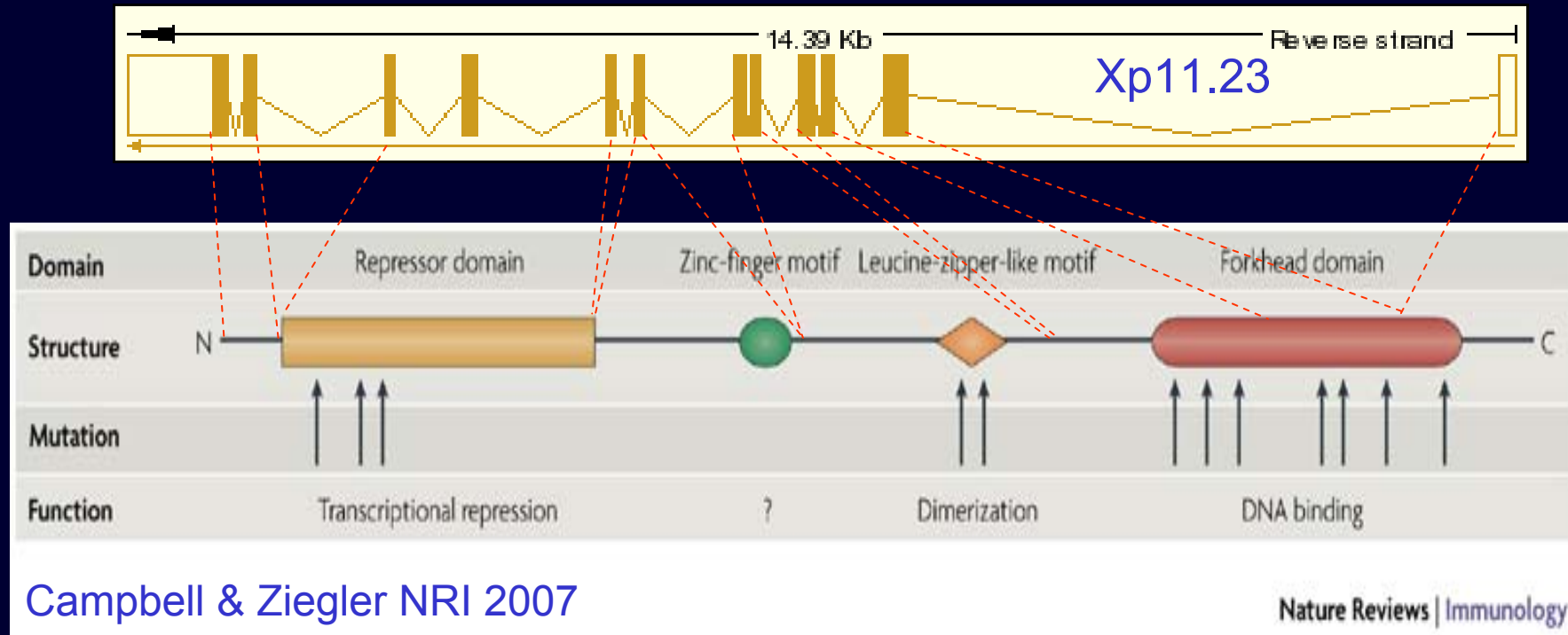
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Regulatory T cells (Treg) and FoxP3 expression

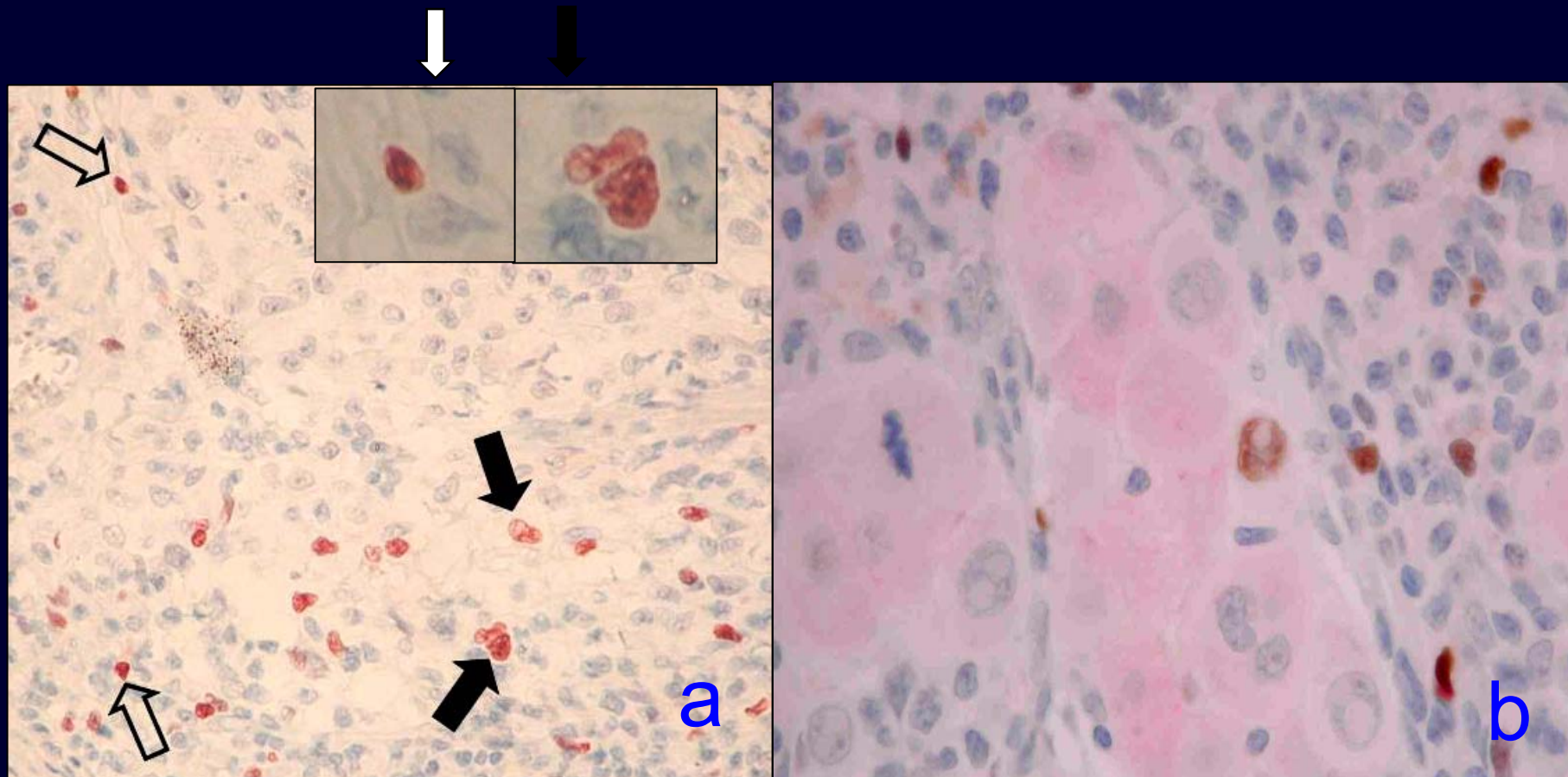
- Immunological homeostasis is maintained by specialized subsets of T cells -- Tregs
- Tregs express FoxP3 – a master transcription factor
- FoxP3 expression in murine CD4+ T cells is necessary and sufficient for their Treg function
- CD4+CD25+ Treg can develop in the absence of FoxP3 (*Lin Nature Immunology p359 2007*)
- Human CD25- T cell can be induced to express FoxP3 and acquire Treg function
- Foxp3 is expressed in pancreatic cancers (*Hinz Cancer Res September 2007*)

FoxP3 gene and its expression



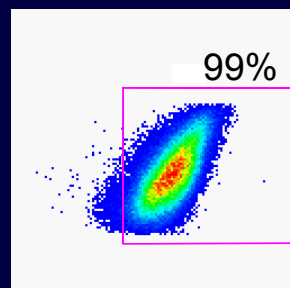
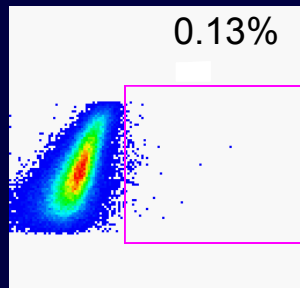
- Human Tregs express two spliced FoxP3
 - Full-length FoxP3
 - FoxP3 Δ 2 (exon 2 deleted) [Allan JCI p3276 2005](#)

FoxP3 expression by lymphocytes and tumour cells in metastatic melanoma tissue

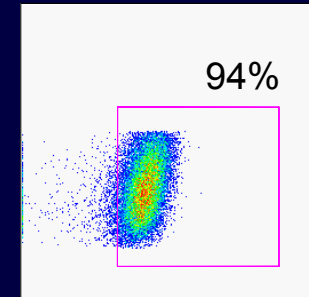
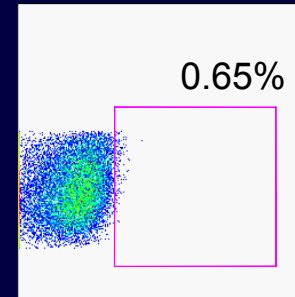


FoxP3 expression in homogenous melanoma cell lines

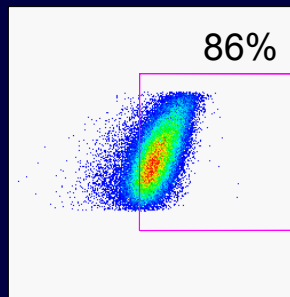
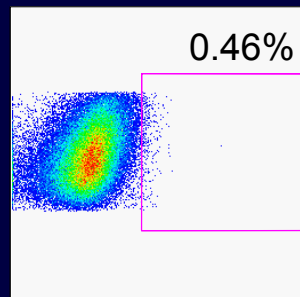
LM-Mel-36
(Melanoma)



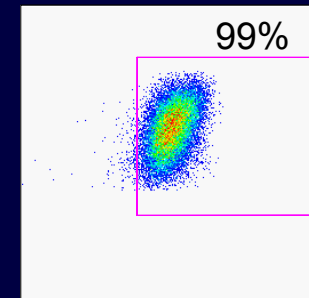
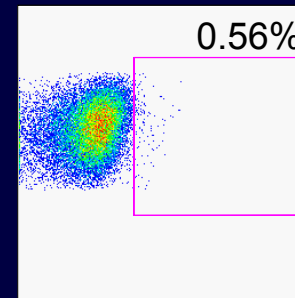
LM-Mel-14
(Melanoma)



LM-Mel-53
(Melanoma)



LM-Mel-26
(Melanoma)



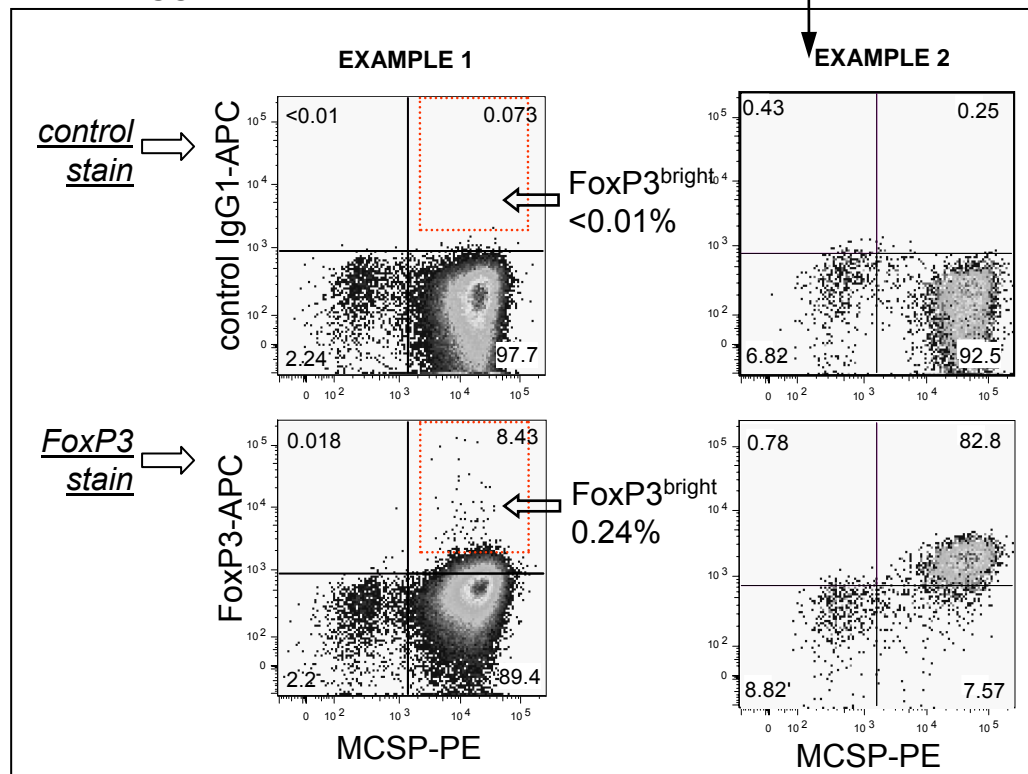
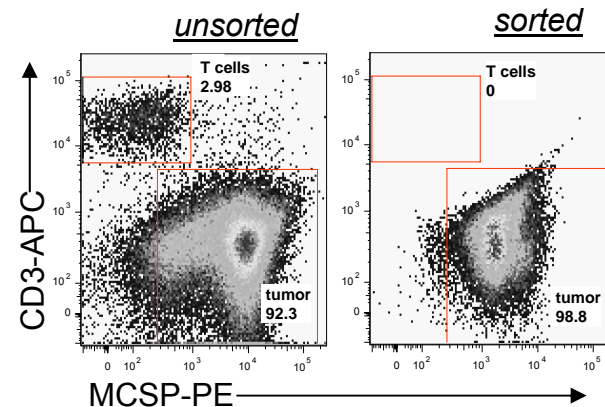
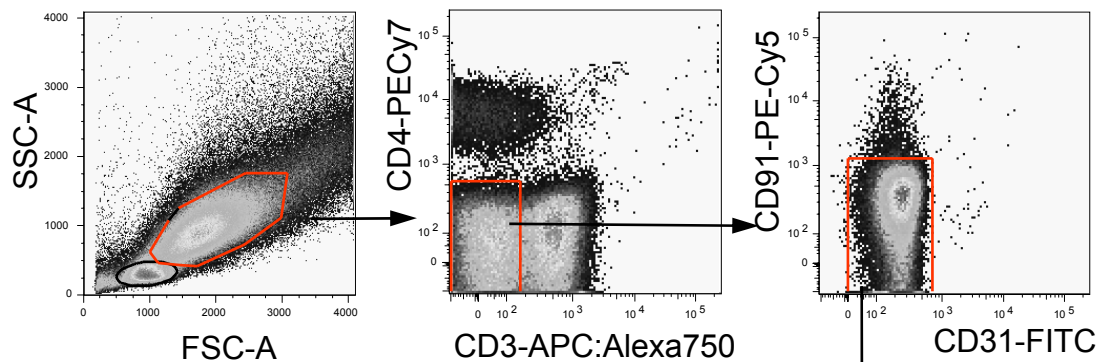
Isotype
Control

FoxP3
236A/E7
ebioscience

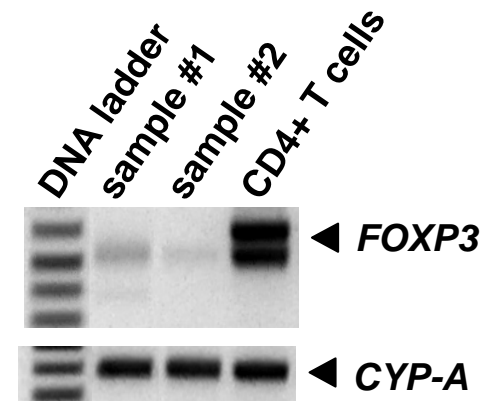
Isotype
Control

FoxP3

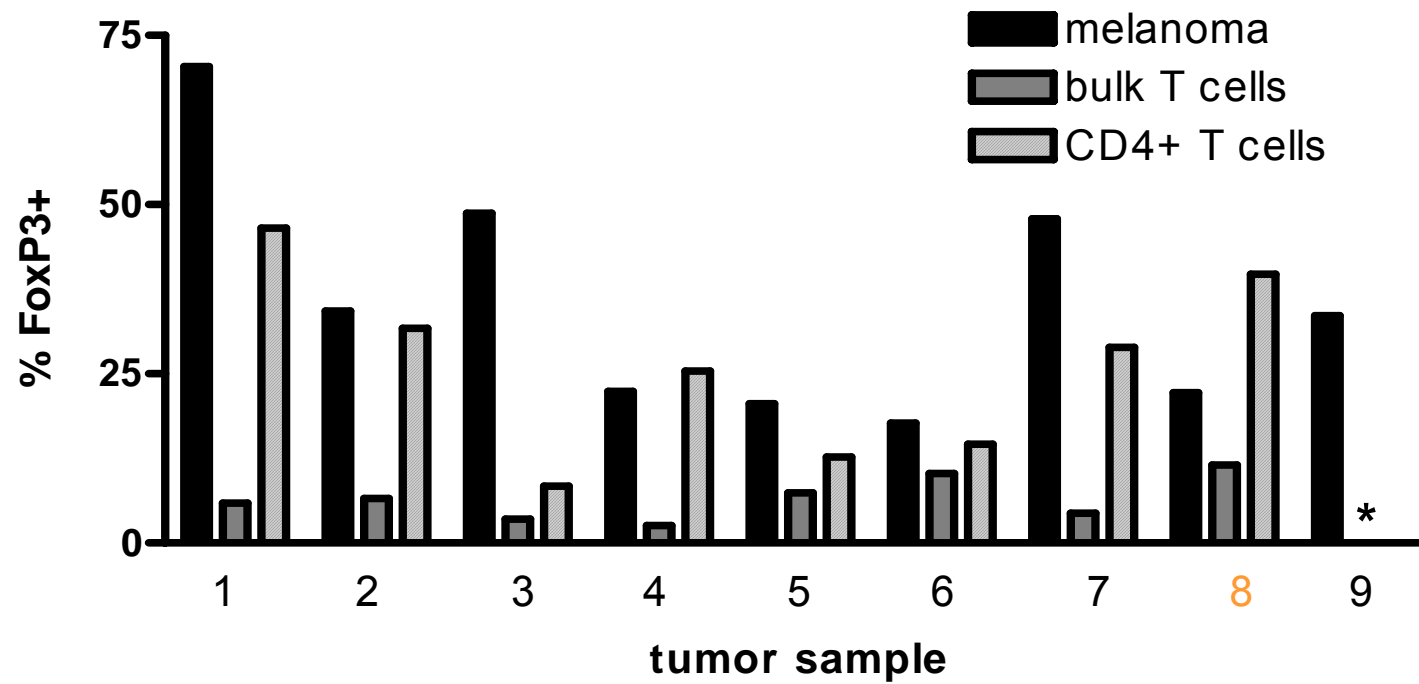
FoxP3 expression in melanoma biopsies



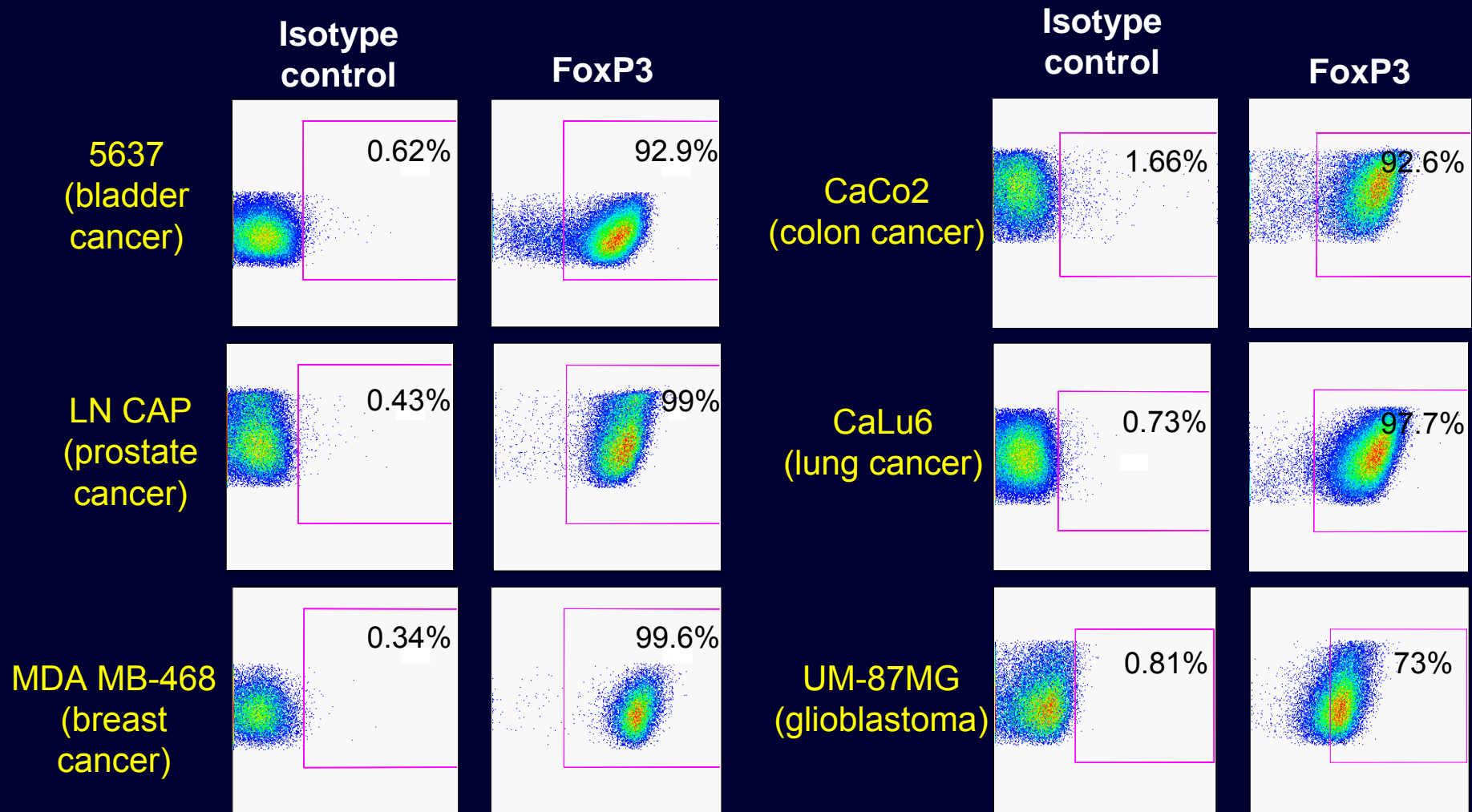
MCSP-melanoma chondroitin sulfate proteoglycan)



FoxP3 expression in melanoma biopsies



What about other tumour types?



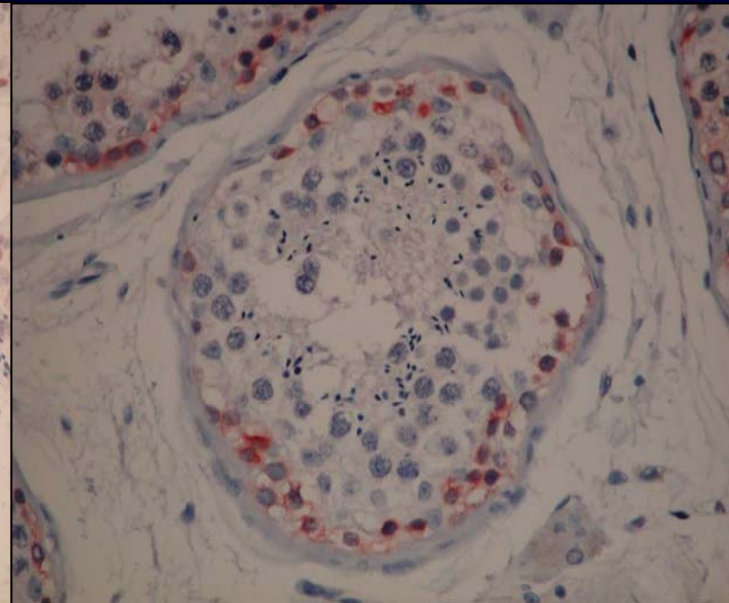
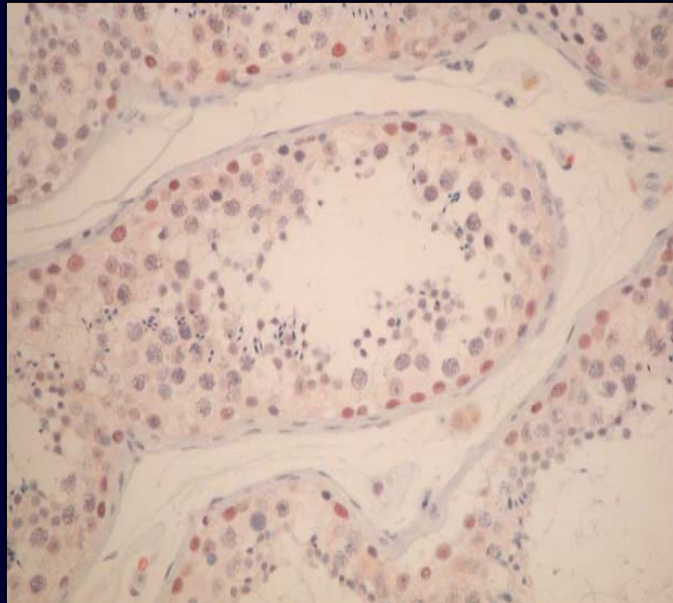
→ confirmed by RT-PCR

FoxP3 expression in testis and placenta

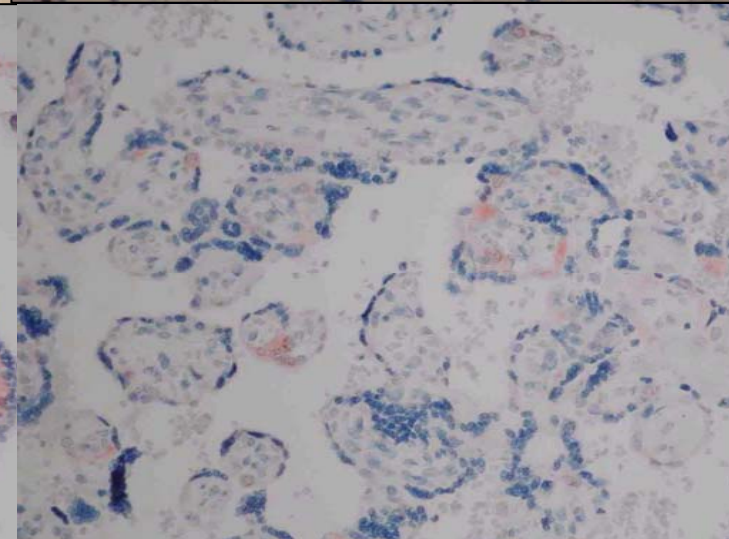
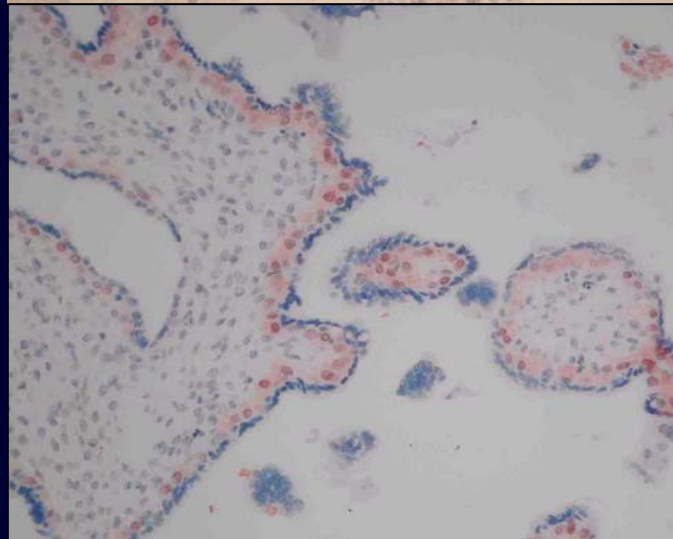
FoxP3

NY-ESO-1

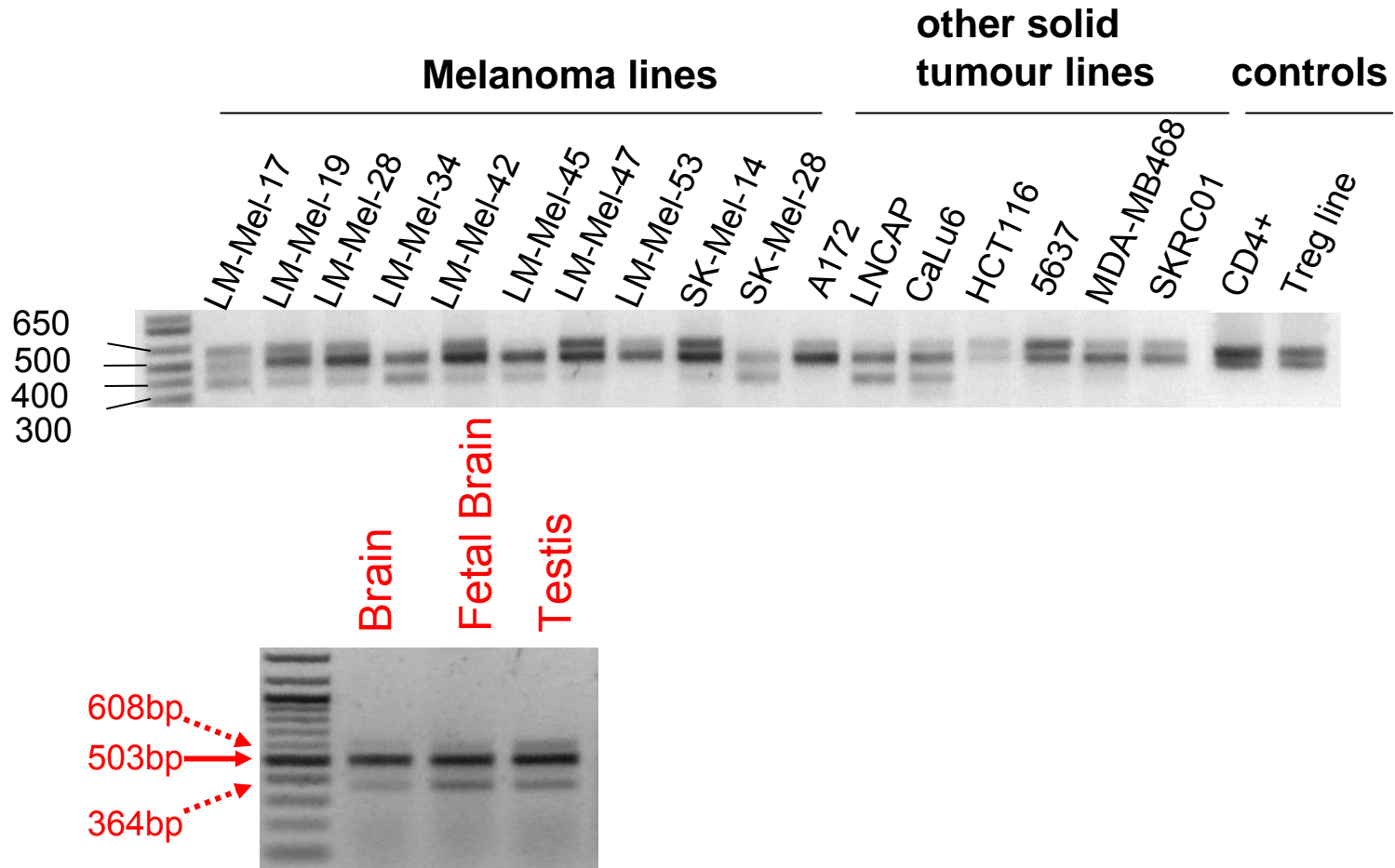
Testis



Placenta



FoxP3 expression in tumour lines by PCR



The novel splice isoform is predicted to encode a very different protein to FoxP3

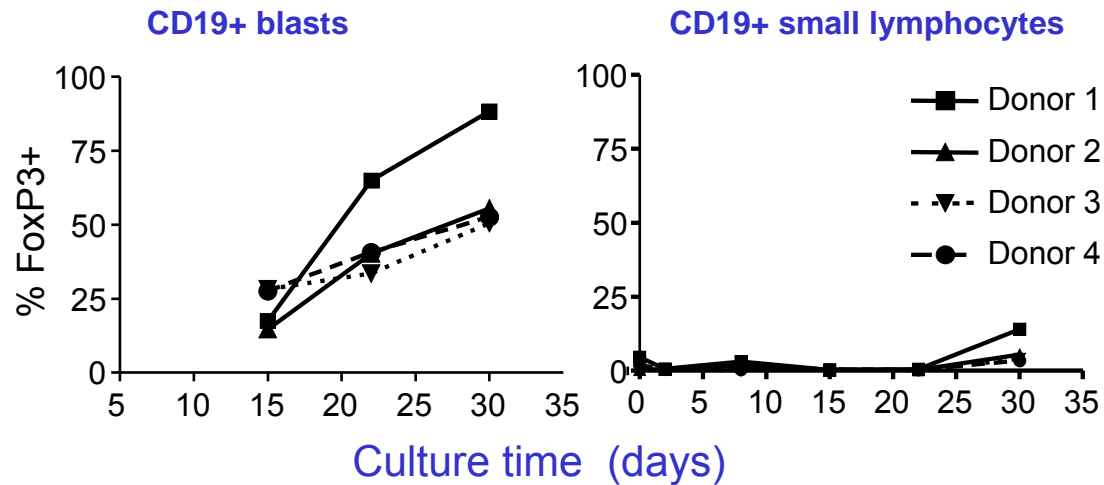
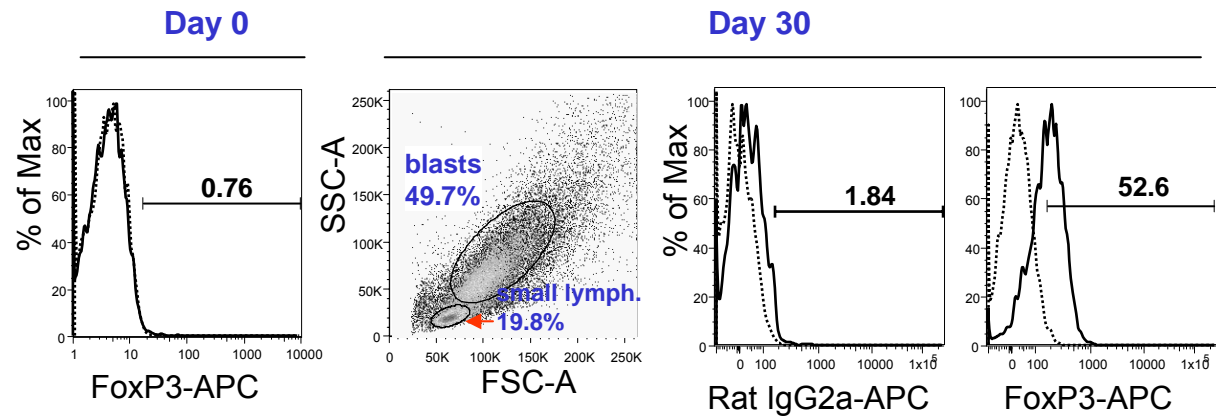
Full-length FoxP3

MPNPRPGKPSAPSLALGPSPGASPSWRAAPKASDLLGARGPGGTFFTQGRDLRGG
AHASSSSLNPMPPSQLQLPTLPLVMVAPSGARLGPLPHLQALLQDRPHFMHFTQL
STVDAHARTPVLQVHPLESPAMISLTPPTTATGVFSLKARPGLPPGINVASLEWV
SRFTEPALLCTFPNPSAPRKDSTLSAVPQSSYPLLANGVCKWPGCEKVFEEPEDF
LKHCQADHFTLLDEKGRAQCLLQREMVQSLEQQLVLEKEKLSAMQAHLAGKMALT
KASSVASSDKGSCCFTIVAAGSQGPVVPAWSGPREADSLFAVRRHLWGSHGNST
FPEFLHNMDYFKFHNMRPPFFTTYATLIRWAILEAPEKQRTLNEIYHWFTRMFAF
FRNHPATWKNAIRHNLSLHKCFVRVEFTSEKGAVWTVDELEFRKKRSQRPSRCSN
PTPGP **(445 AA)**

Predicted $\Delta 2\Delta 3$ isoform

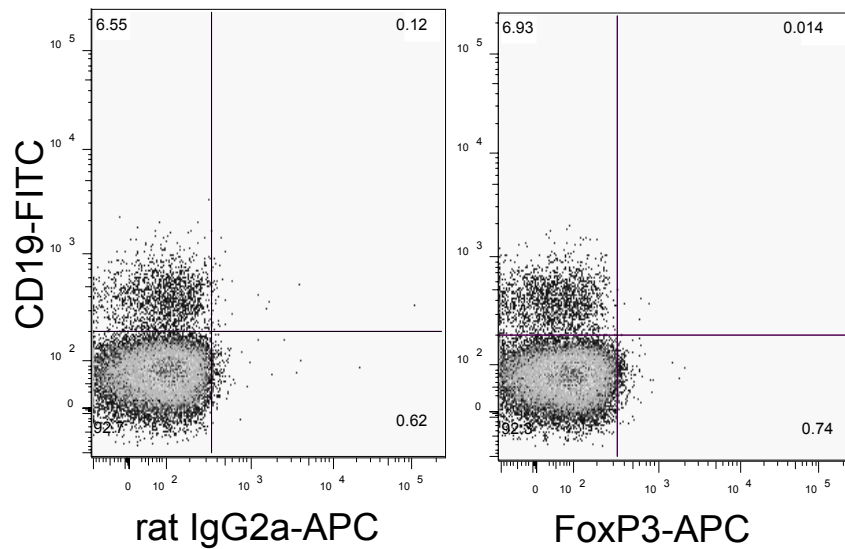
MPNPRPGKPSAPSLALGPSPGASPSWRAAPKASDLLGARGPGGTFFQGRDLRGGAH
ASSSSLNPMPPSQLQ**GSTWPAWNGCPGSRHCSAPSQIPVHPGRTAPFRLCPRAPT**
HCWQMVSASGPDVRRSSKSQRTSSSTARRTIFWMRRAGHNVSSRERWYSLWSSSW
CWRRRSZ (171 AA)

FoxP3 expression in EBV transformed B cells

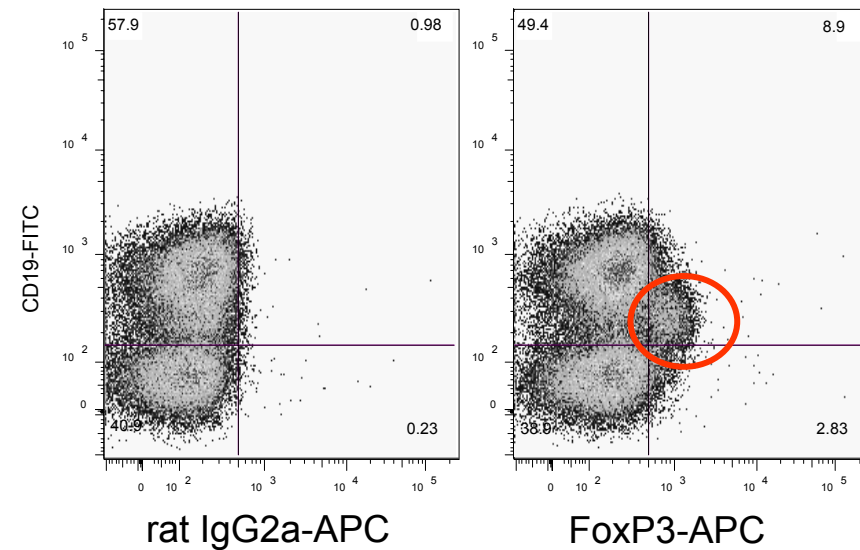


FoxP3 expression in an EBV-caused PTLD patient (post-transplant lymphoproliferative disorder)

PBMC



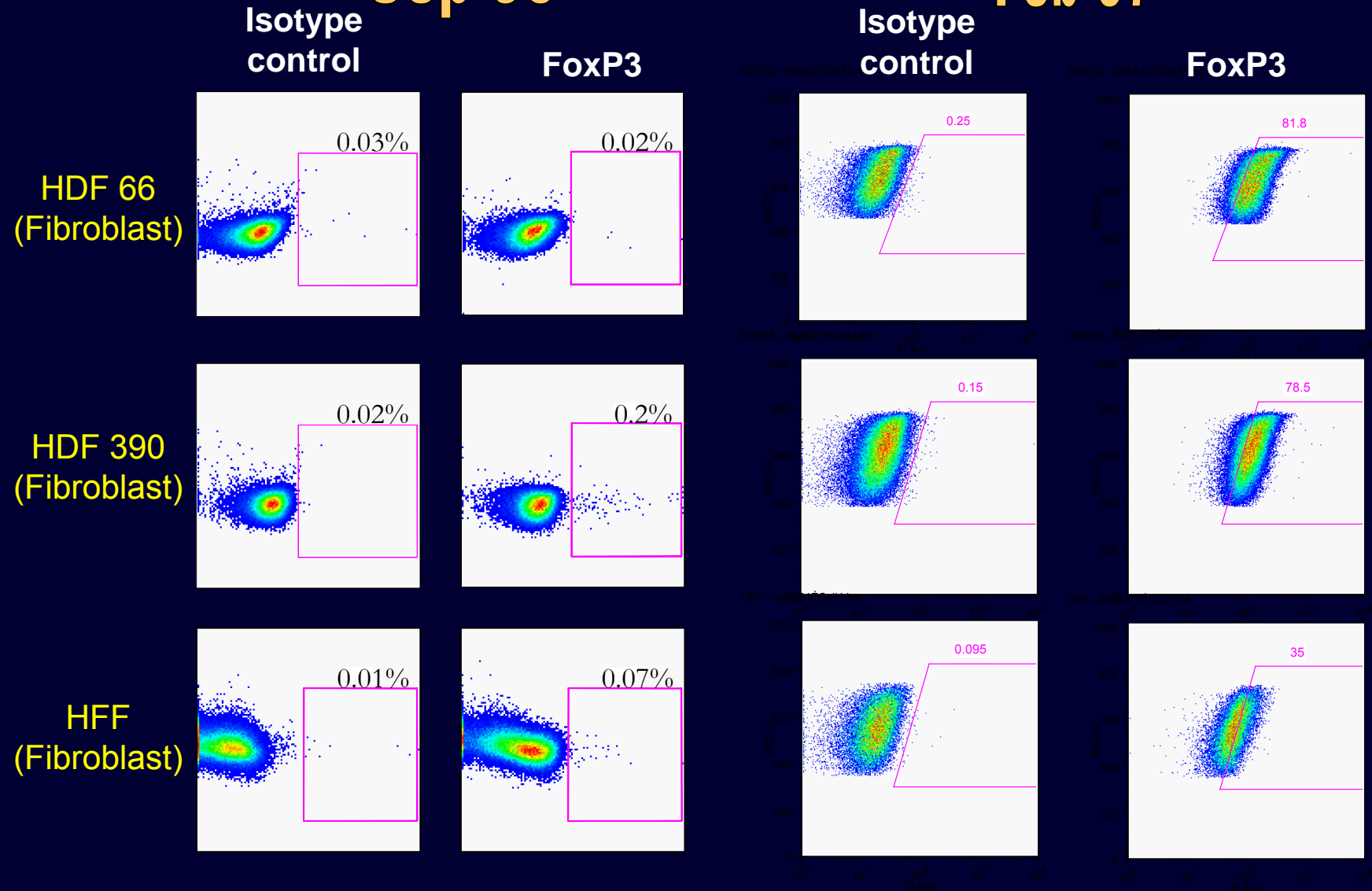
Tumour cells



Induced FoxP3 expression in fibroblast cell lines

Sep 06

Feb 07



Induced FoxP3 expression in fibroblast cell lines

Sep 06

Feb 07

Fibroblast

Endothelial

Monocyte-derived
Dendritic cells

B-cells

HDF32
HDF66
HDF390
HFF
HUVEC
HMVEC
Donor1
Donor2
Donor3
Donor1
Donor2
Donor1
Donor2
PCR water

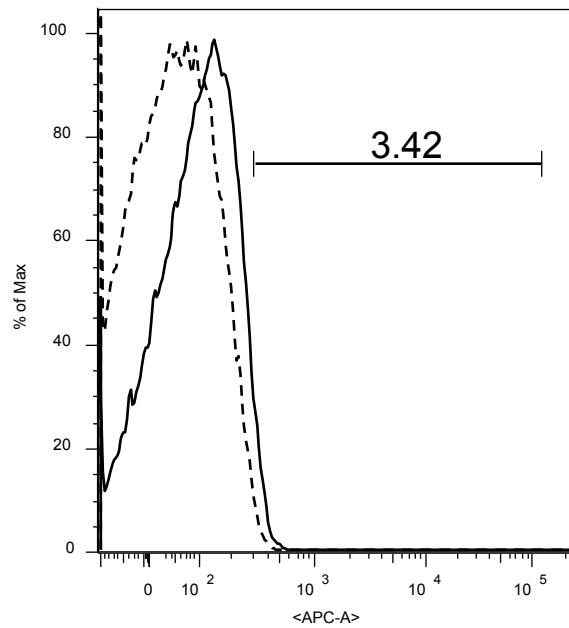


HDF32
HDF66
HDF390
HFF
HUVEC
Treg

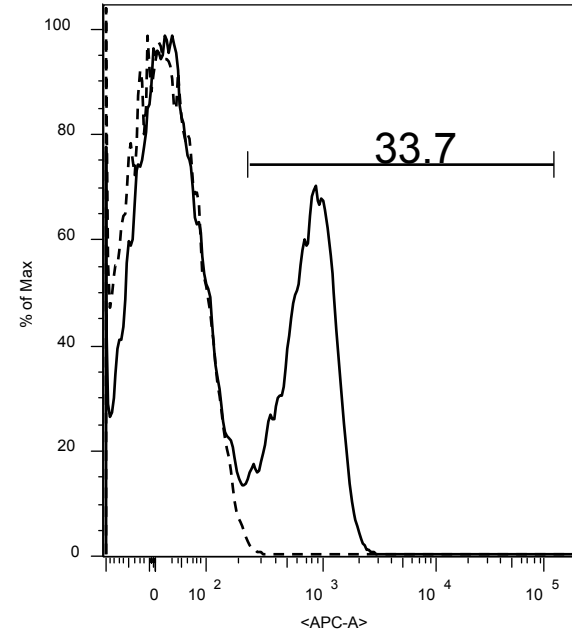


FoxP3 is not expressed in murine tumours

B16 melanoma



CD4+ splenocytes

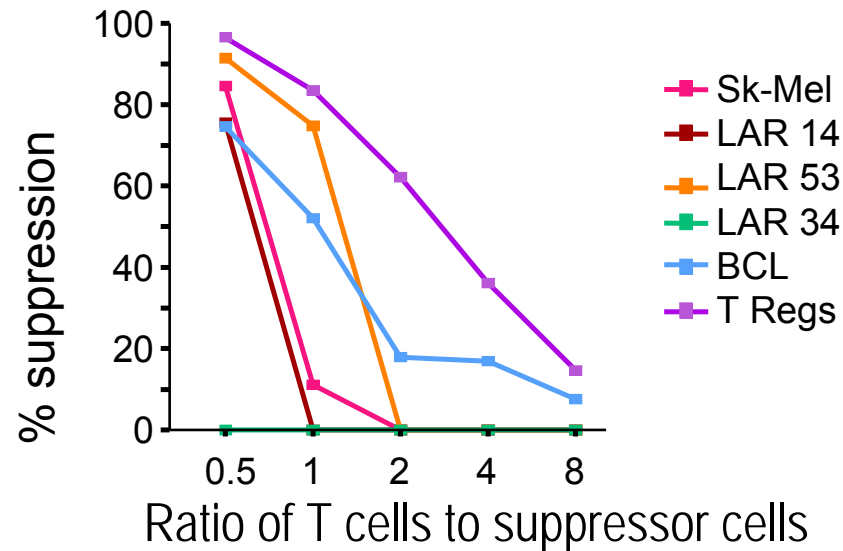
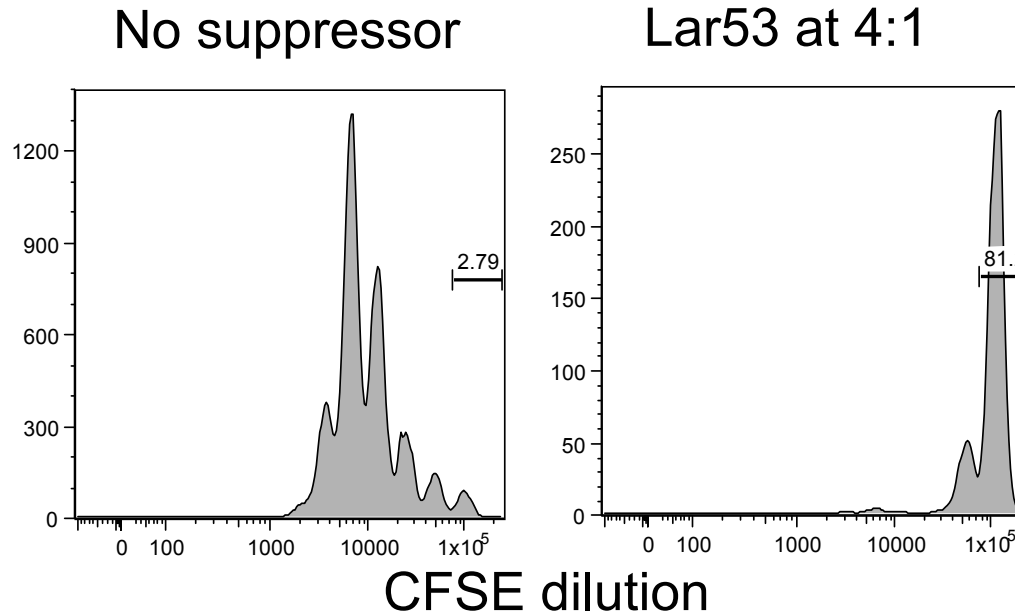
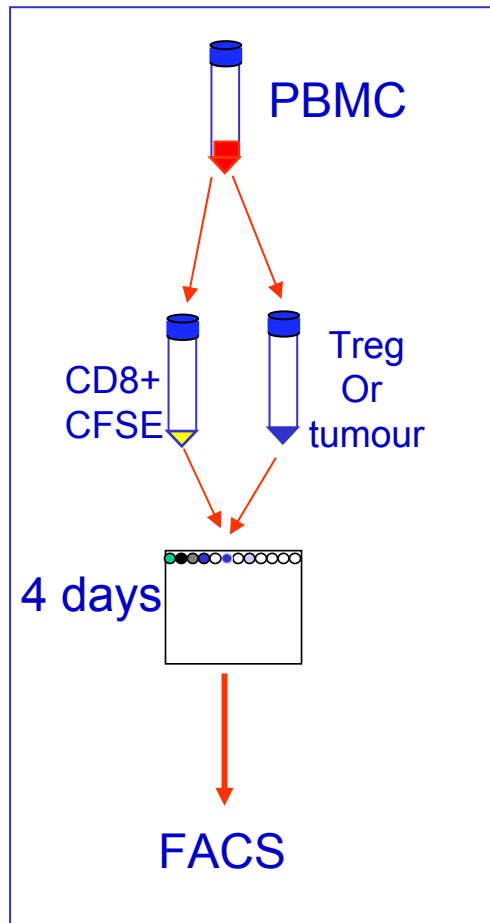


FoxP3-APC

Why FoxP3 expression in tumour, transformed cells and germ cells?

- Convey immune privilege?
- Suppressing T cells to escape immune surveillance?

Can tumour cells suppress T cells in vitro?



To take home...

- FoxP3 is expressed by various tumour cell lines
- FoxP3 is expressed by some tumour cells (TIL) in tumour biopsies
- FoxP3 is expressed by EBV-transformed B cells in vitro and in vivo
- FoxP3 is expressed by cells at the immune privilege sites
- A novel FoxP3 splice isoform is detected in tumours and immune privilege sites, but not in Treg

ACKNOWLEDGEMENT

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