Table 1S. Distribution of P-Smad2 staining scores in SCC, by patient age, gender, OTR status and relative sun exposure of body site.

Patient	**P-Smad2 expression levels in SCC**				
Feature	**Low**	**Medium**	**High**	**Total**	**P-value, χ^2**
Age					
< 70	31 (36%)	27 (31%)	28 (32%)	86	0.241
> 70	30 (39%)	30 (39%)	16 (21%)	76	
Gender					
Male	48 (40%)	40 (33%)	33 (27%)	121	0.941
Female	13 (33%)	15 (25%)	11 (28%)	39	
OTR Status					
Non-OTR	39 (47%)	30 (36%)	13 (16%)	82	< 0. 001
OTR	22 (27%)	27 (33%)	32 (39%)	81	
Tumor Site					
Sun-protected	26 (43%)	21 (35%)	13 (21%)	60	0.486
Sun-exposed	35 (36%)	34 (34%)	29 (30%)	98	

∗ Sun-protected areas are defined as the trunk, arms, legs and feet regions. Sun-exposed areas are defined as head, neck, wrist and hand regions. The differences between the groups were tested by $\chi 2$ analysis.

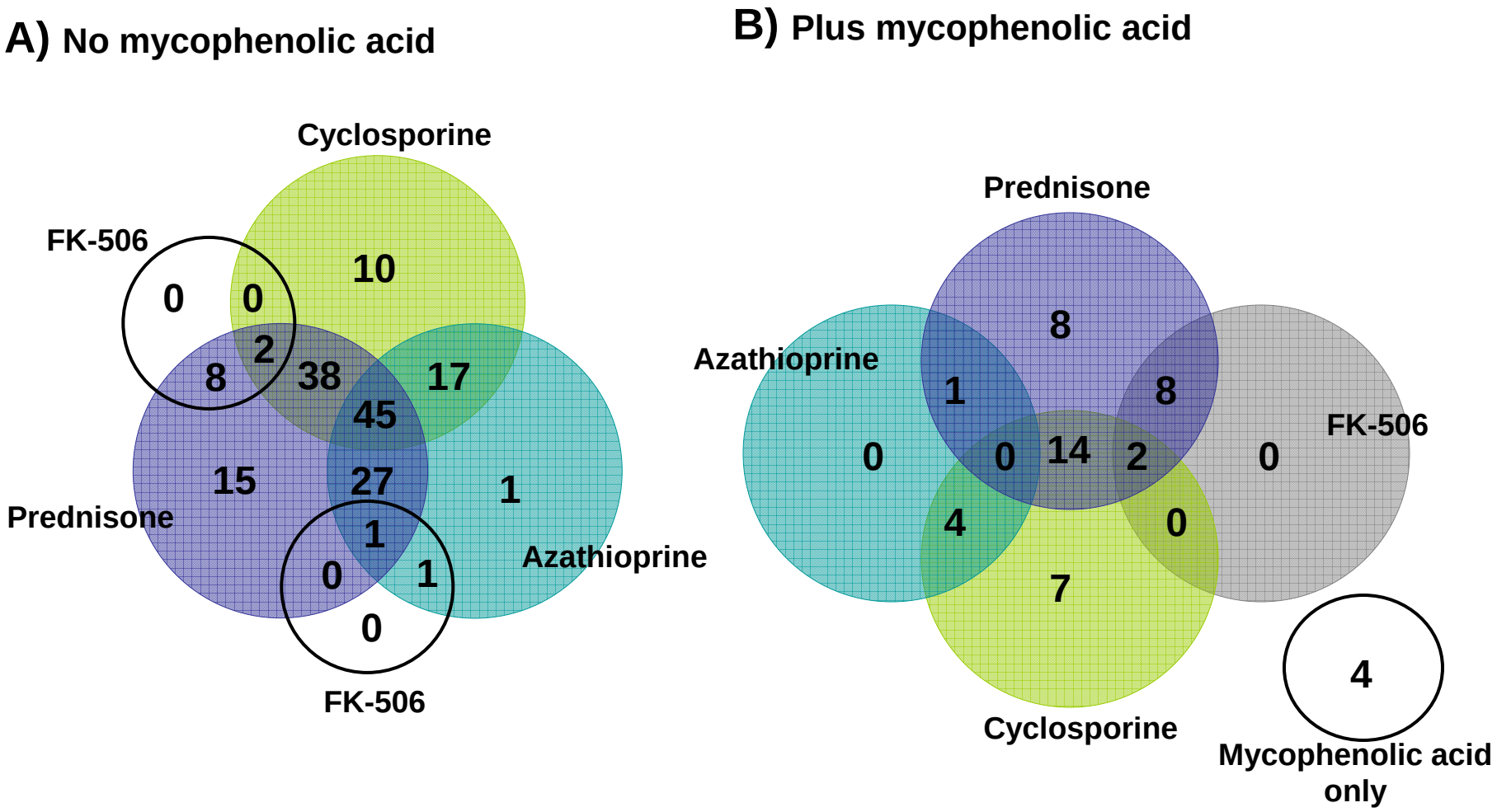
Figure 1S. Spectrum of OTR drug regimens. Venn diagrams indicate the range of drug cocktails that patients received for at least 6 months prior to each skin lesion excision. Number represent individual tissue samples (in some cases this included adjacent non-lesional skin). A) Patients did not receive mycophenolic acid treatment prior to lesion excision; B) Patients were also receiving mycophenolic acid therapy prior to lesion excision.

Figure 2S. Age distributions in non-OTR versus OTR patients with SCC. a) Boxplots show median age (horizontal line in box) and interquartile range (25th to 75th percentile) for OTR and non-OTR patients. The mean age in the non-OTR group is 75 years with standard deviation of 13. OTR group had a mean age of 59 years with a standard deviation of 11. There was a significant difference between age groups ($P < 0.001$, T-test).
b) P-Smad2 staining intensity data are plotted as dots. Locally weighted linear regression (LOWESS) fits P-Smad2 staining intensity as a function of patient age. When intensity was regressed on age for each type of tumor (OTR or non-OTR) neither was significant ($P = 0.84$ for OTR and $P = 0.90$ for Non-OTR). Thus, the age difference shown in Figure **2Sa** does not significantly affect stain intensity in the two patient categories, OTR and non-OTR.

Figure 3S. P-Smad2 staining is reduced in SCCs compared to adjacent non-lesional skin. Non-lesional skin (a), its adjacent SCC (b) and a less differentiated SCC (c), stained with the anti-P-Smad2 antibody. Unstained haemotoxylin positive nuclei in (b) and (c) are infiltrating leukocytes (Arrow). Arrow heads point to carcinoma cell nuclei that are strongly P-Smad2 positive. (d) and (e) show low power images of these SCCs and their adjacent skins (thin arrows) to illustrate the differential in P-Smad-2 staining from skin and tumor. Thick

arrow indicates position of core punched out for microarray. Boxes in (d) and (e) indicate relative positions of images captured in a-c.

Figure 4S. TGF-β2 and TGF-β3 levels are similar in SCC and non-lesional skins samples from OTRs and non-OTRs. Tissue microarrays were stained for TGF-β2 and TGF-β3. A) and B) show representative images of distinct cores at A) × 10 and B) × 40 magnifications. C) Individual cores were scored as to staining intensity. The percentage of samples in each staining category was plotted for OTRs and non-OTRs. The number of independent patient specimens contributing to the data is shown on the x axis. There were no and significant differences between OTRs and non-OTRs.



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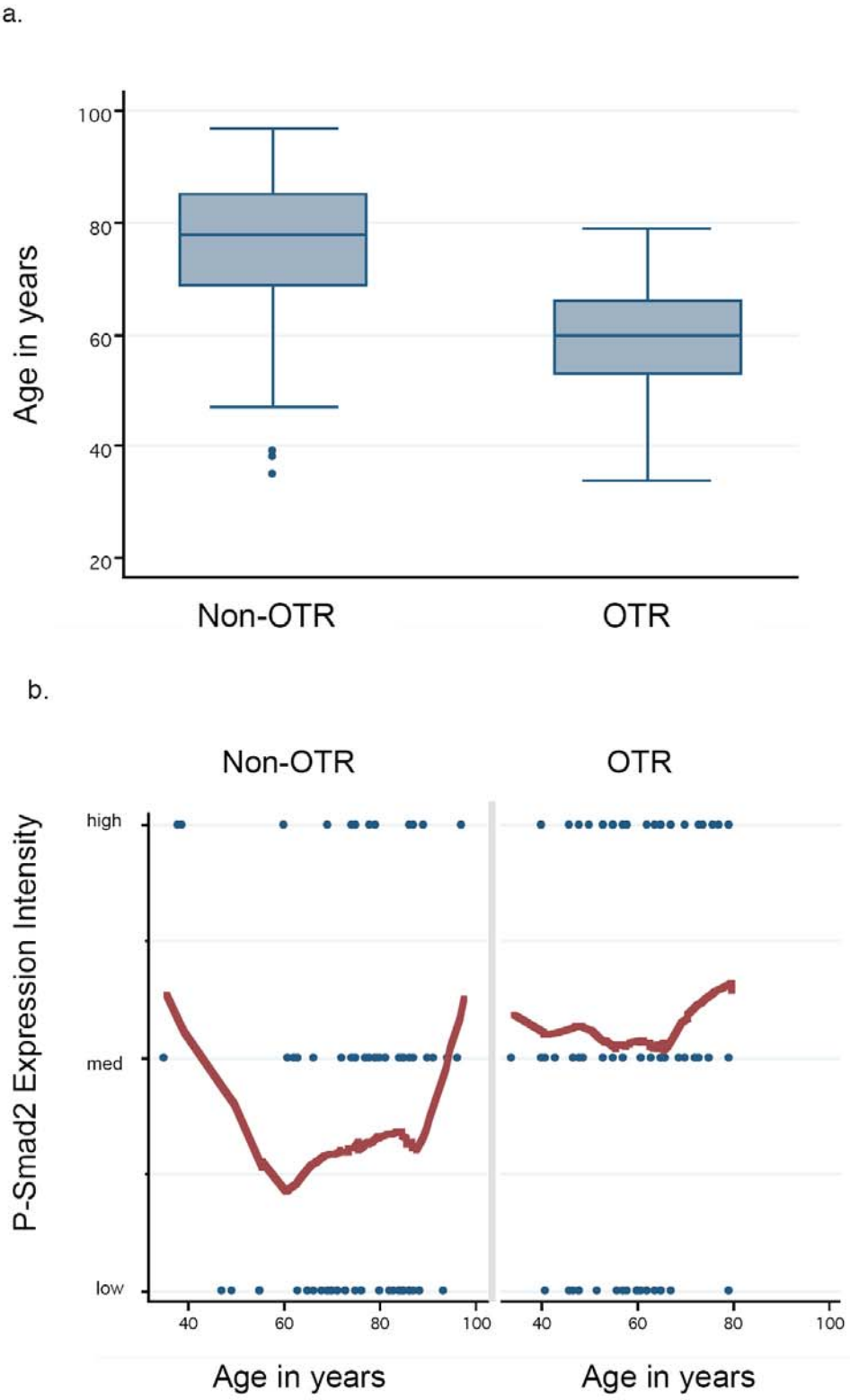

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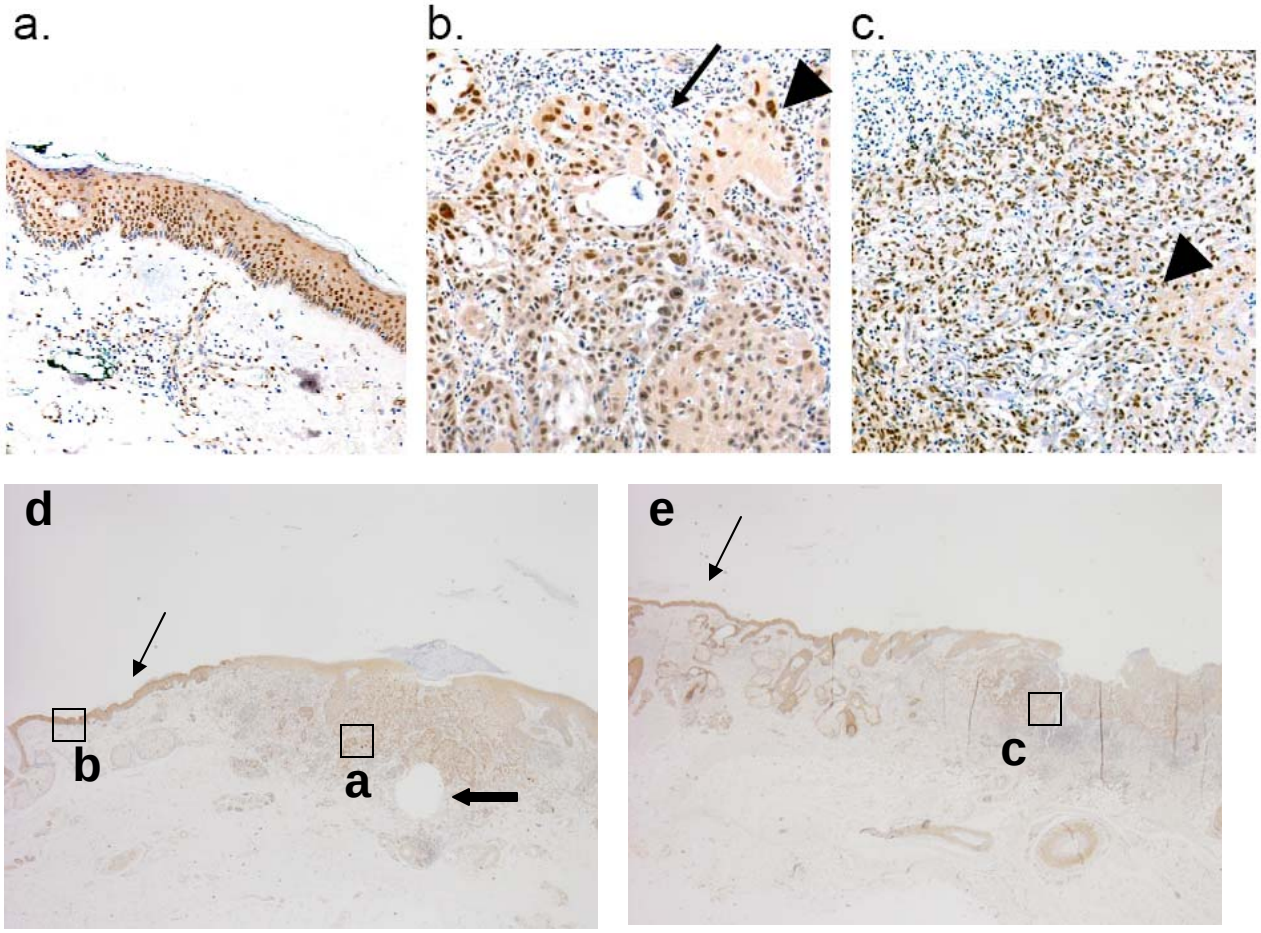

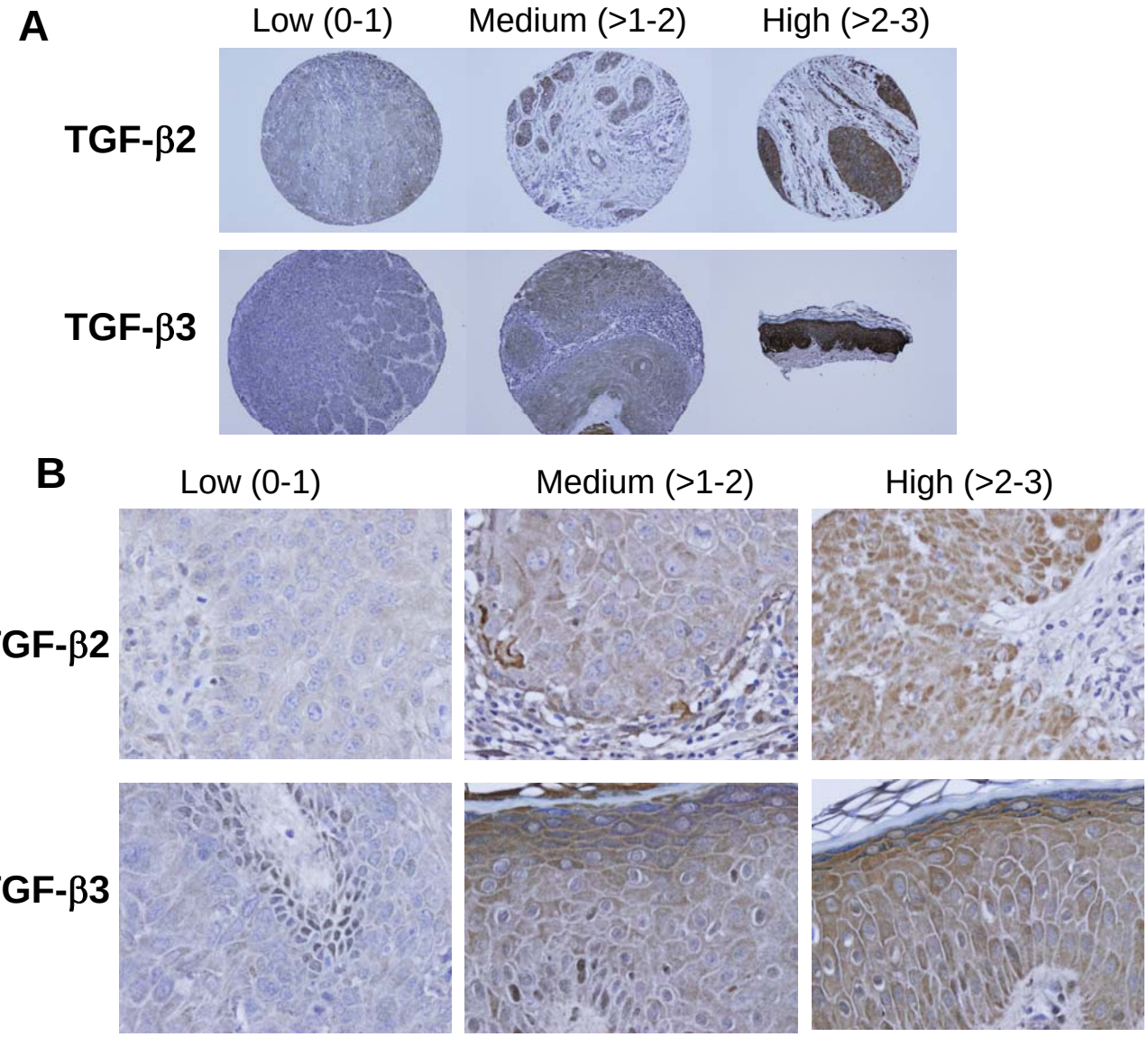
A
Low (0-1)
Medium (>1-2)
High (>2-3)
TGF-β2
TGF-β3
B
Low (0-1)
Medium (>1-2)
High (>2-3)
TGF-β2
TGF-β3
C
TGFβ2
TGFβ3
Normal skin
SCC
Normal skin
SCC
100%
80%
60%
40%
20%
0%
% of samples
0-1
>1-2
>2-3
Non-OTR (28)
OTR (17)
Non-OTR (81)
OTR (64)
Non-OTR (26)
OTR (15)
Non-OTR (76)
OTR (56)