

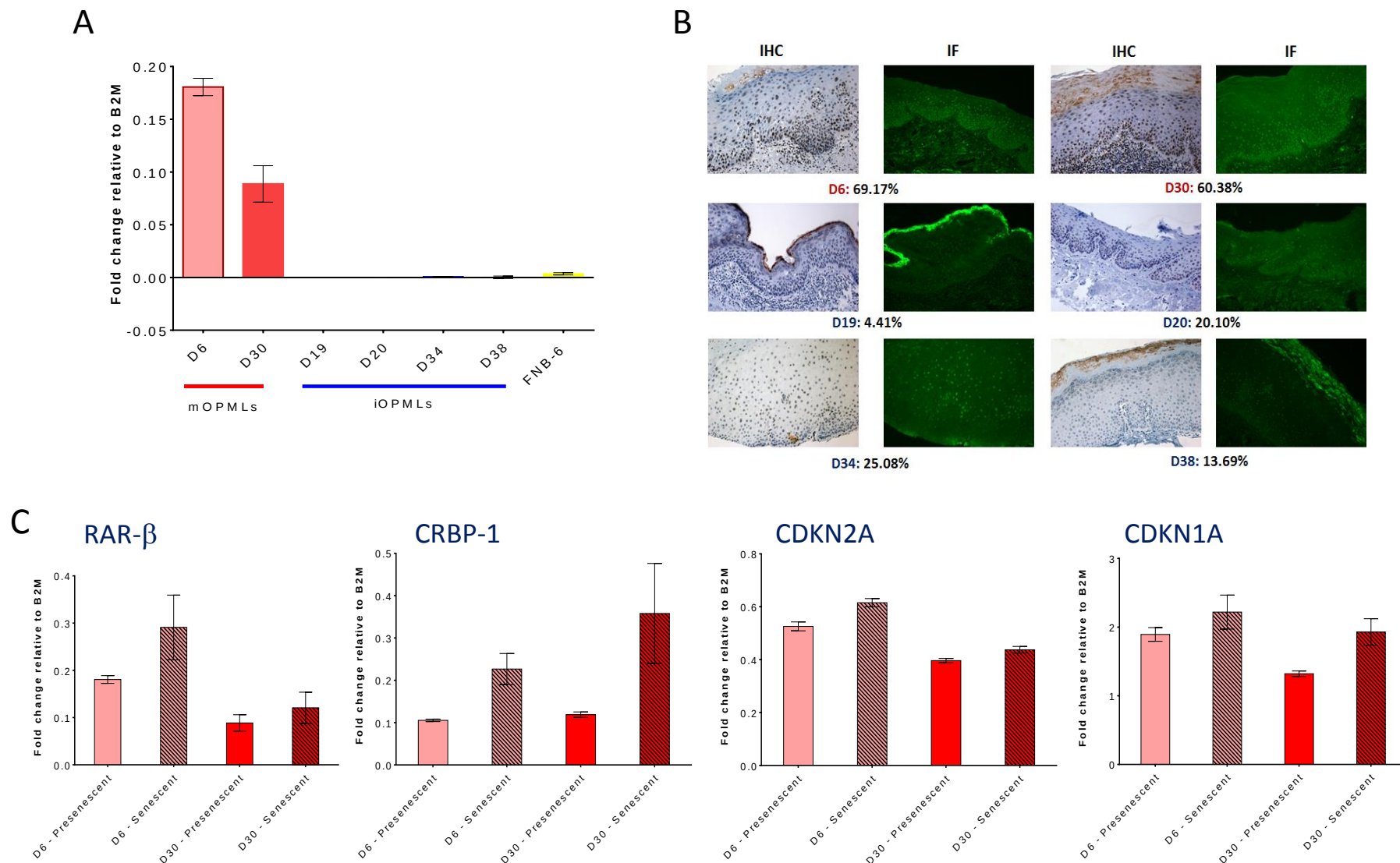
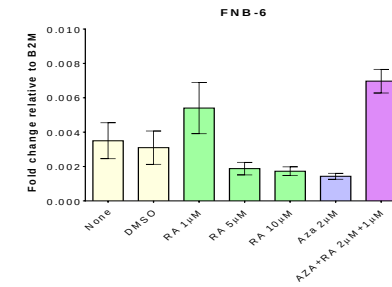
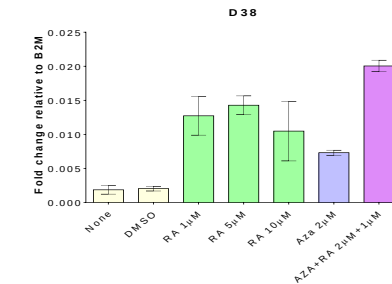
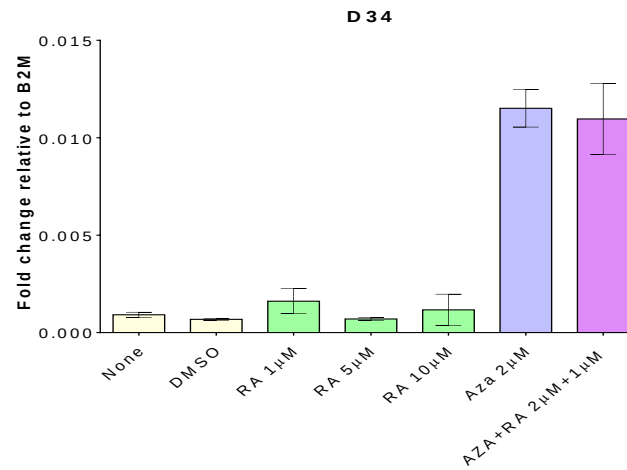
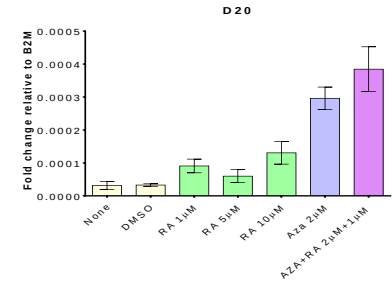
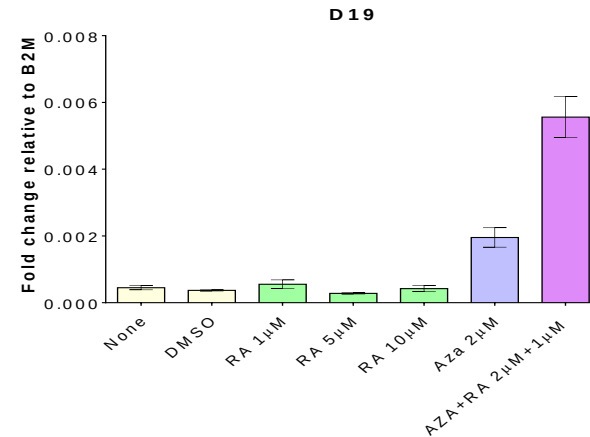
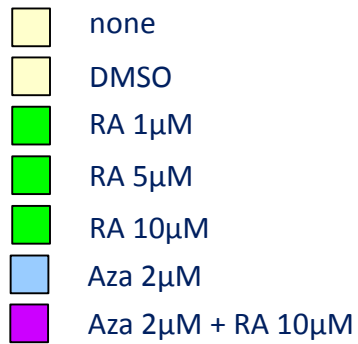


Figure 1. RAR β is downregulated in OPML cells (A) and matched tissues (B). RAR β is constitutively expressed in mOPMLs (D6 and D30) and low in iOPMLs (D19, D20, D34, D38) and iNOKs. RAR β 2 is more highly expressed in MDs at senescence (C).

Treatment schedule



MS-PCR

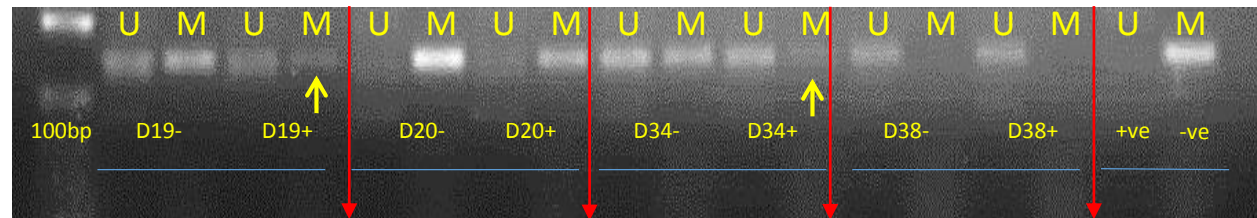


Figure 2: RAR β 2 is re-expressed in iOPMLs following treatment with RA and Aza-C. Promoter methylation was confirmed by MS-PCR and sequencing.

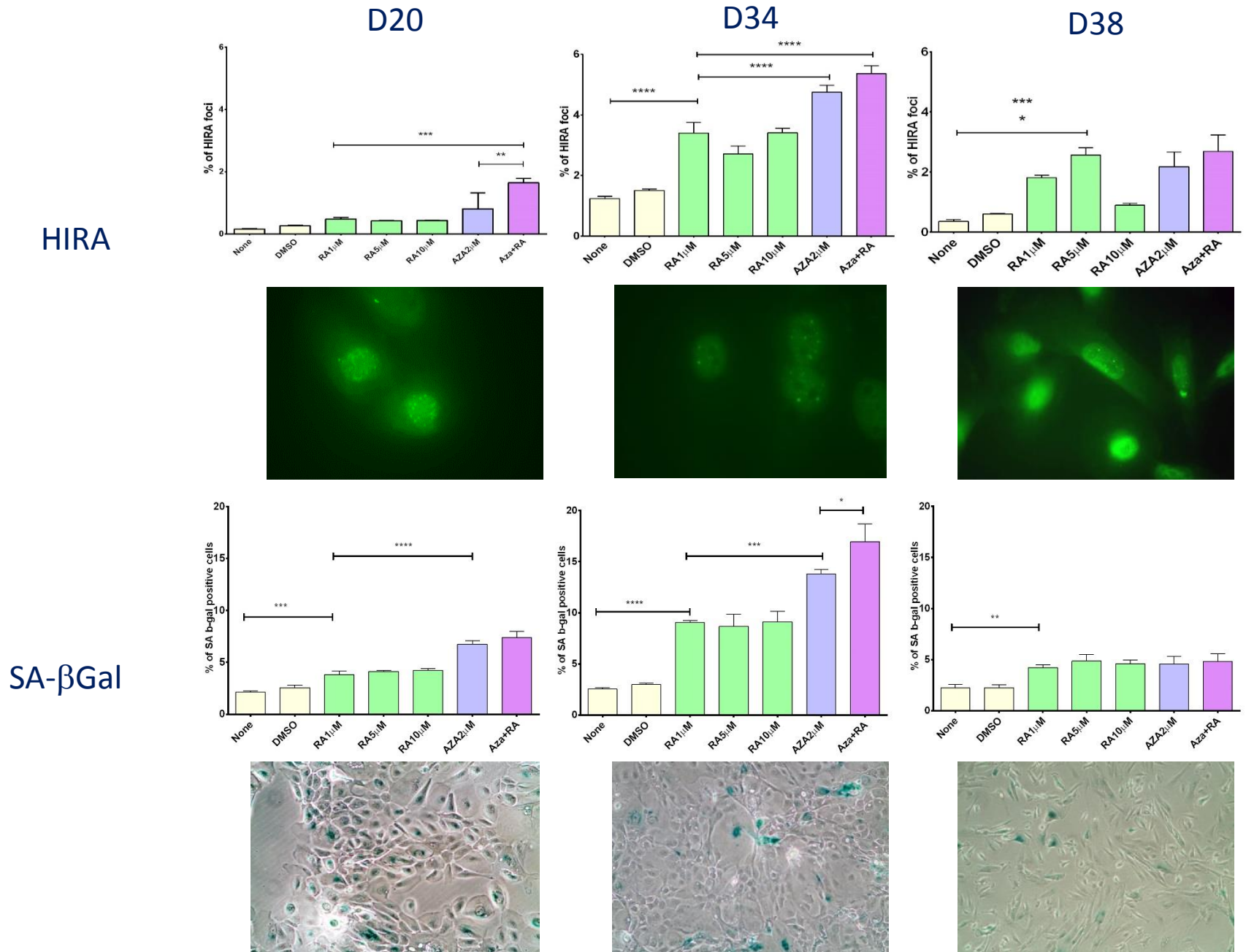


Figure 3: Treatment with RA and Aza-C increases the proportion of cells showing features of senescence

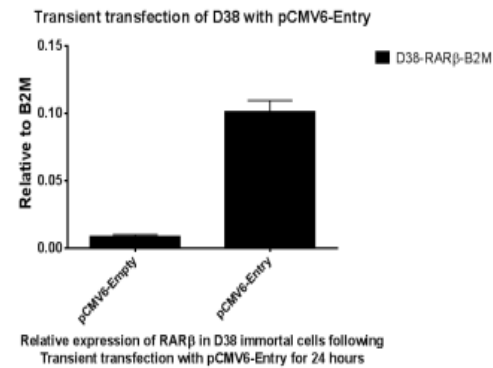
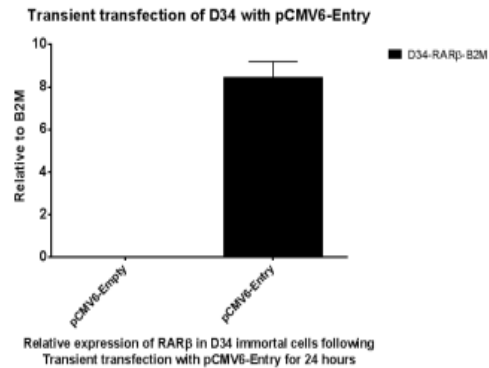
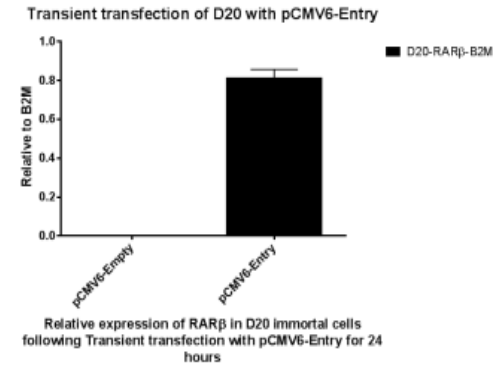
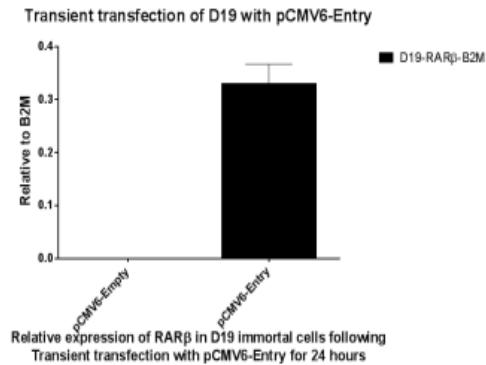


Figure 4: Relative expression of RARβ2 in immortal cells following transient transfection with pCMV6- entry TrueORF Gold Clone for 48 hours

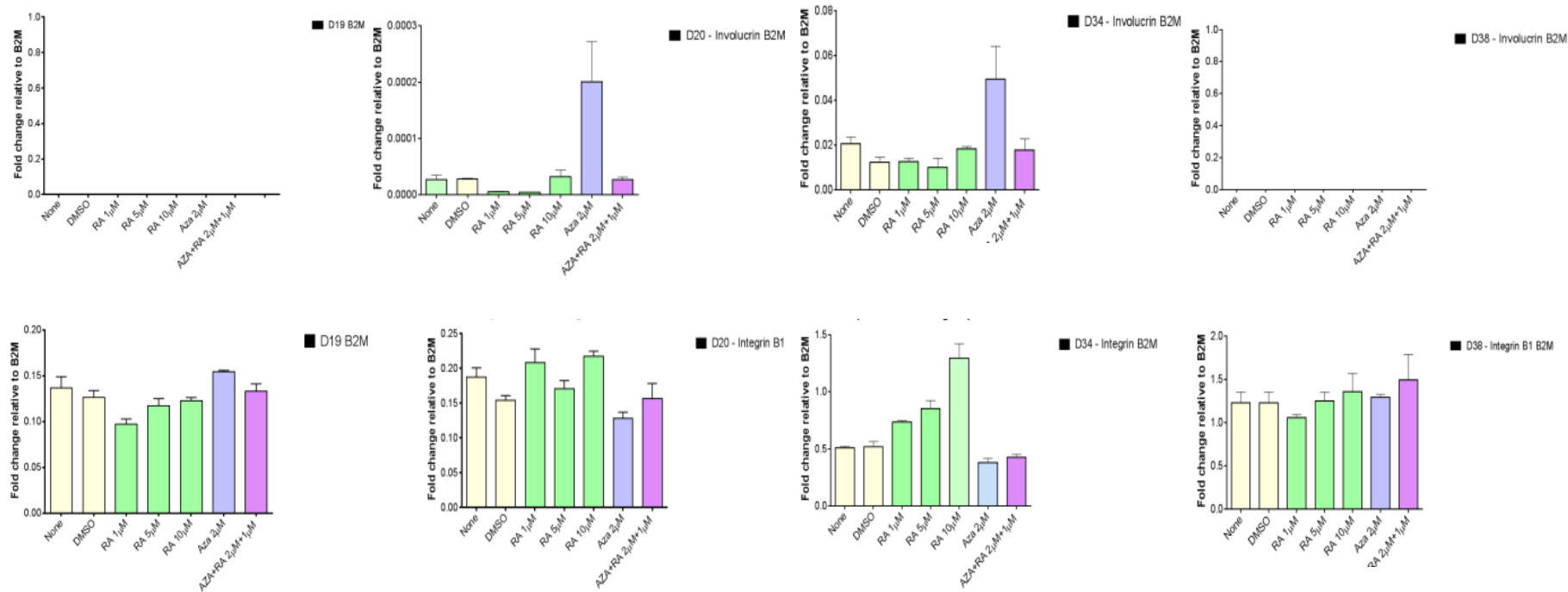


Figure 5. Expression of Involucrin (upper panels) and ITGB1 (lower panels) after treatment as per schedule

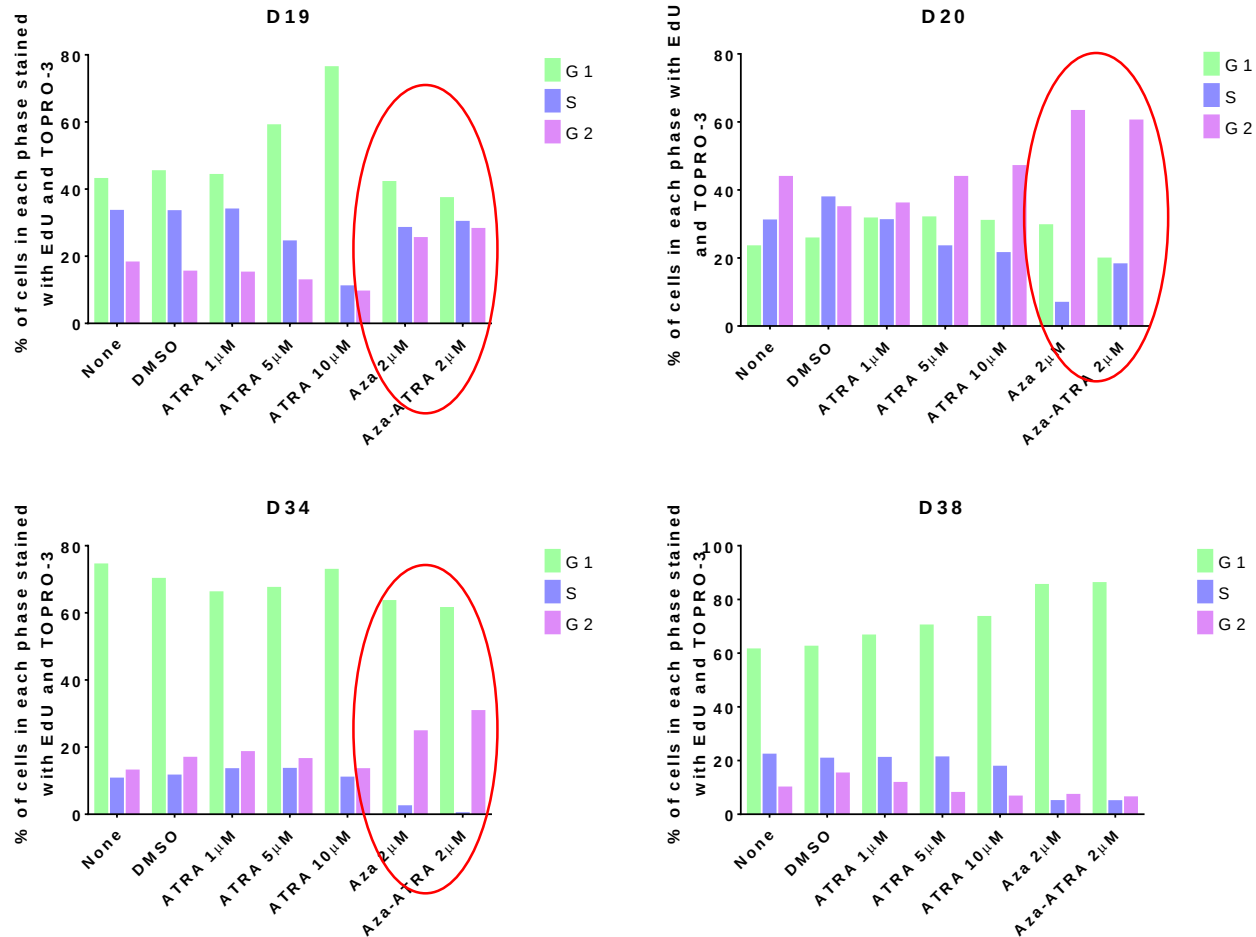


Figure 6: Cell cycle analysis shows that there is G2/M arrest in some OPML cells on Aza-C treatment. As shown by EdU incorporation there is a slowdown of cell turnover with RA and block in G2M phase with Aza-C and Aza-C + RA.

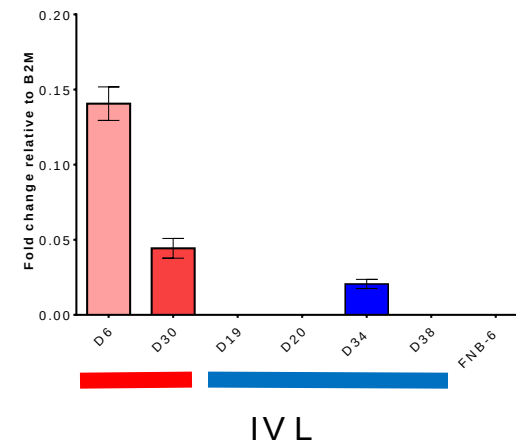
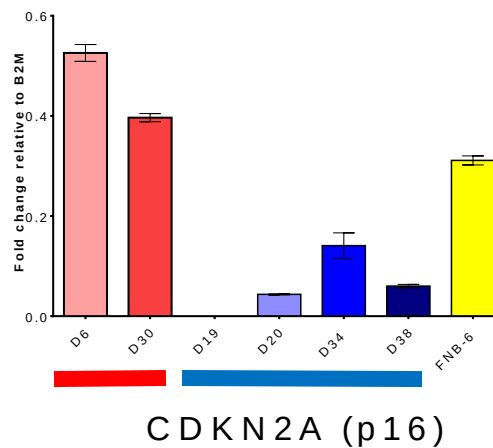
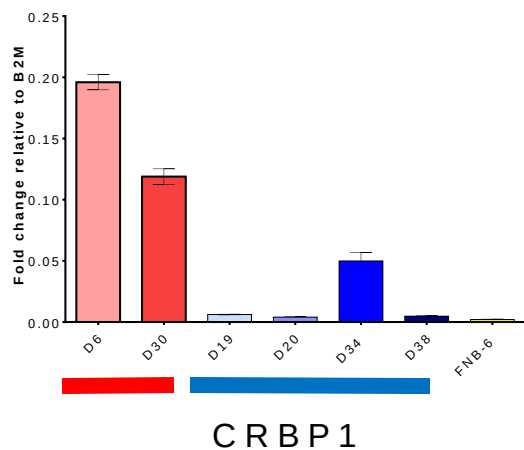
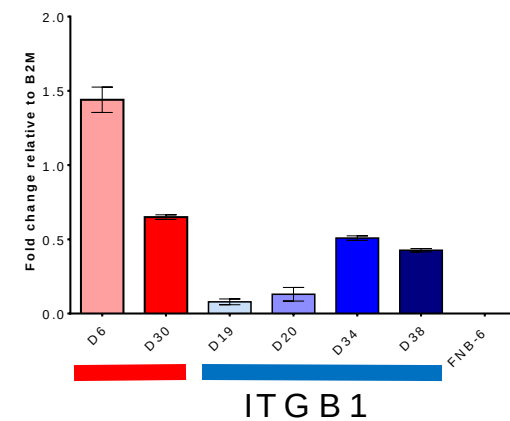
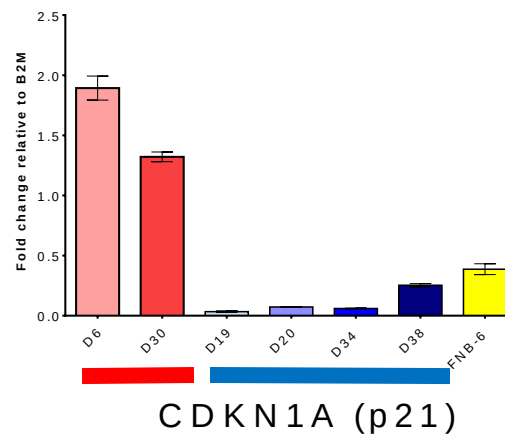
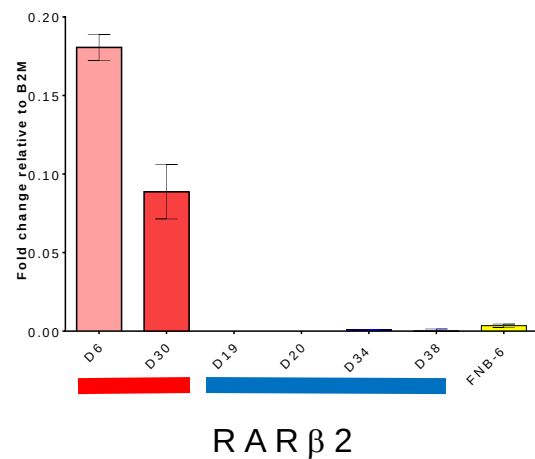
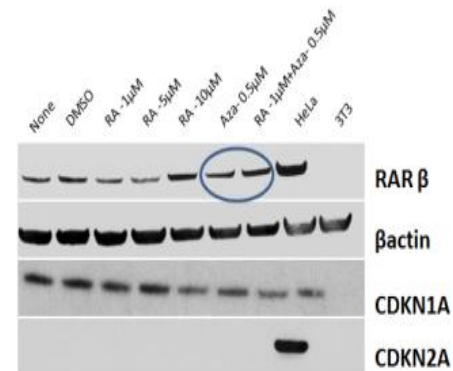
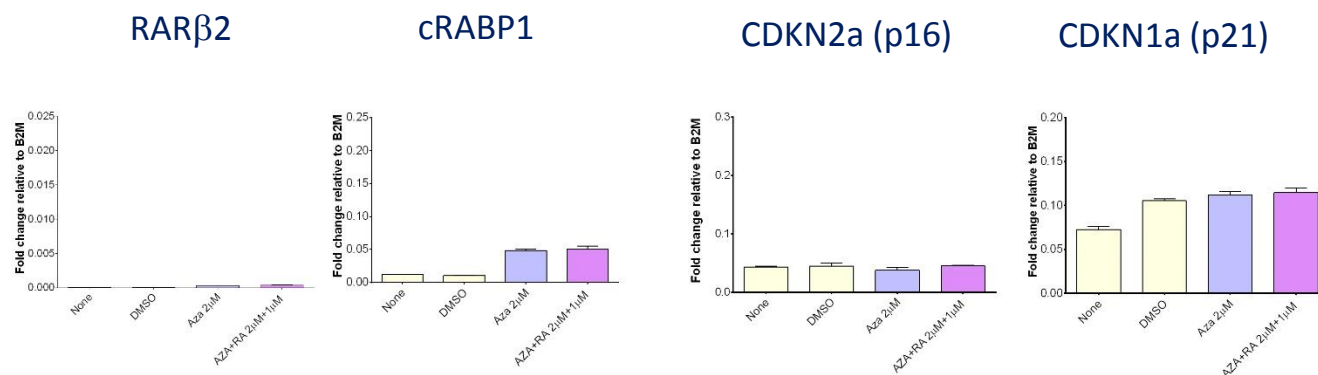
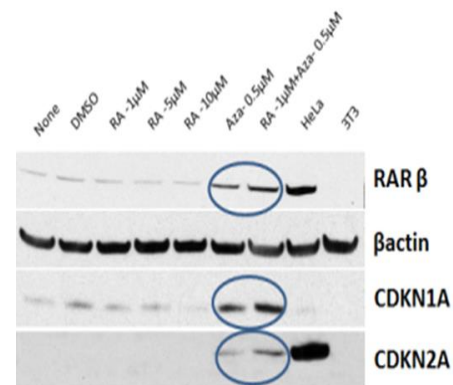
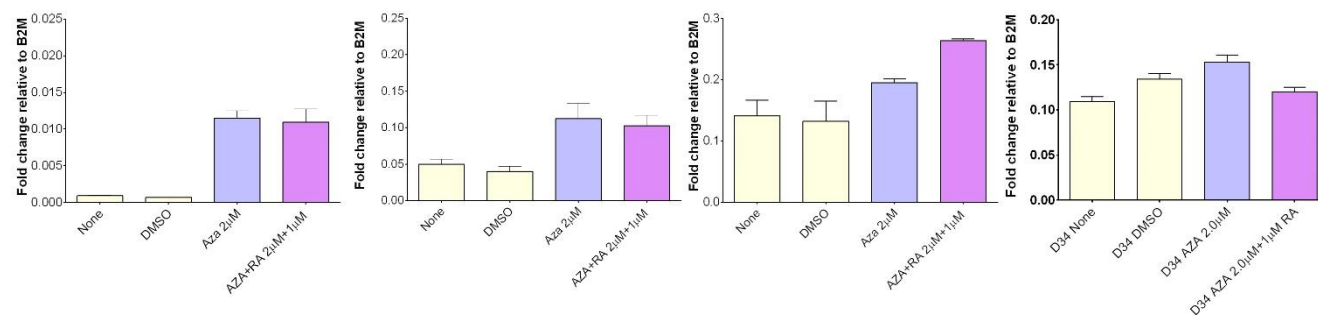


Figure 7A: RAR β 2 expression is linked to abnormalities in cell cycle and differentiation markers

D20



D34



D38

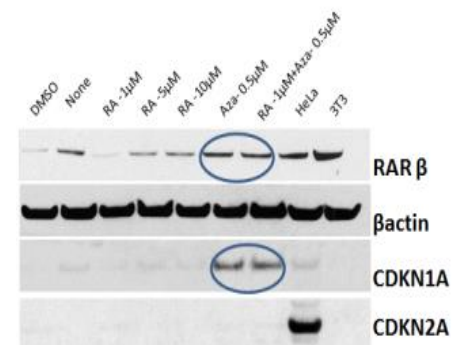
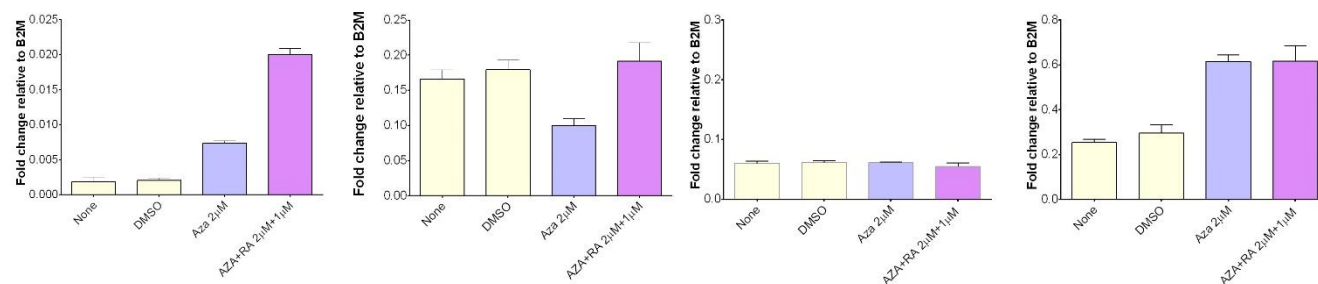


Figure 7B: AZA-C and RA treatment also affects cRBP1, CDKN2a and CDKN1a expression. The pattern of expression in D19 is very similar to that in D34

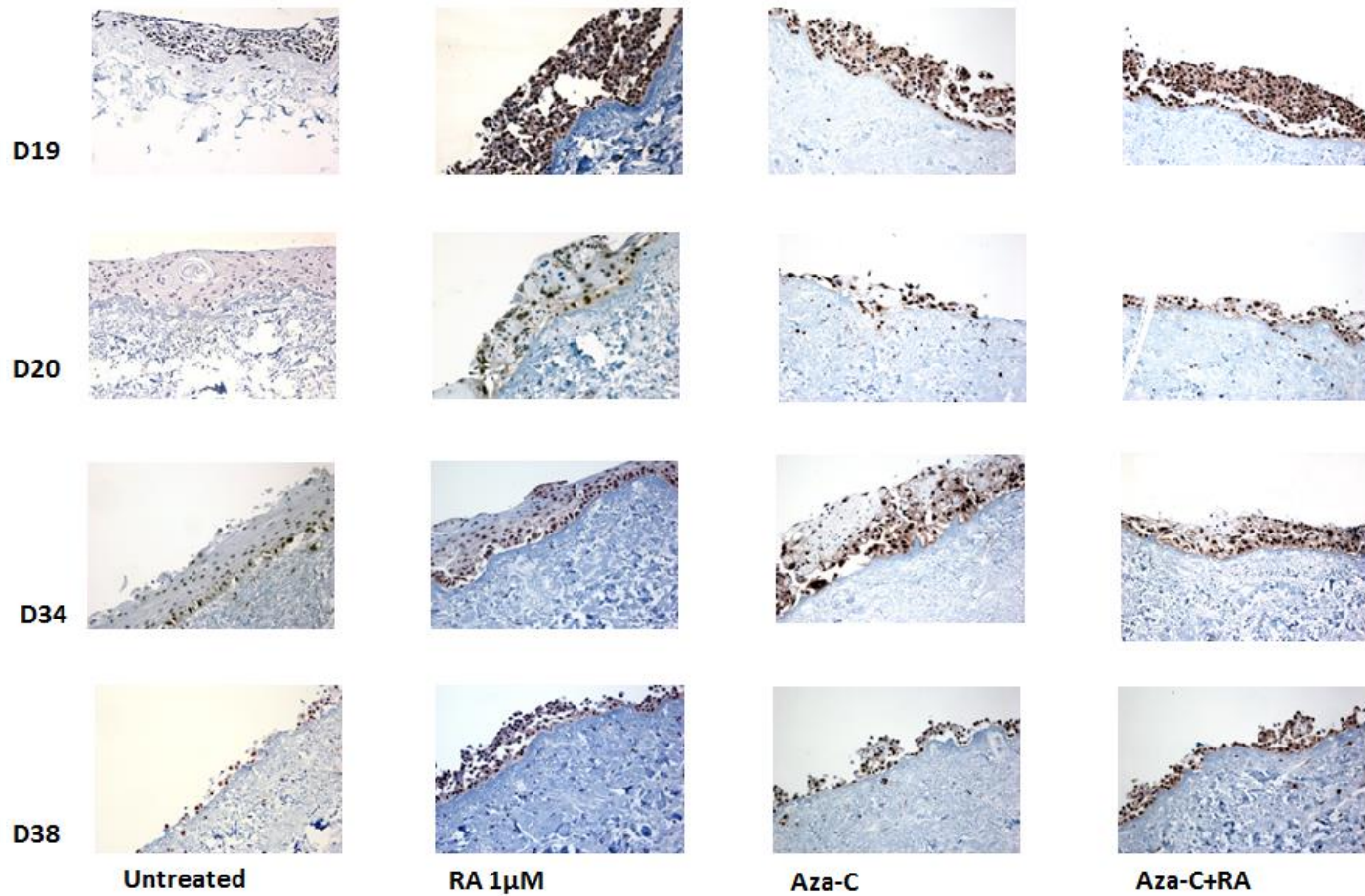


Figure 8. RAR β expression increases in tissue engineered oral mucosal models on treatment with RA and Aza-C + RA

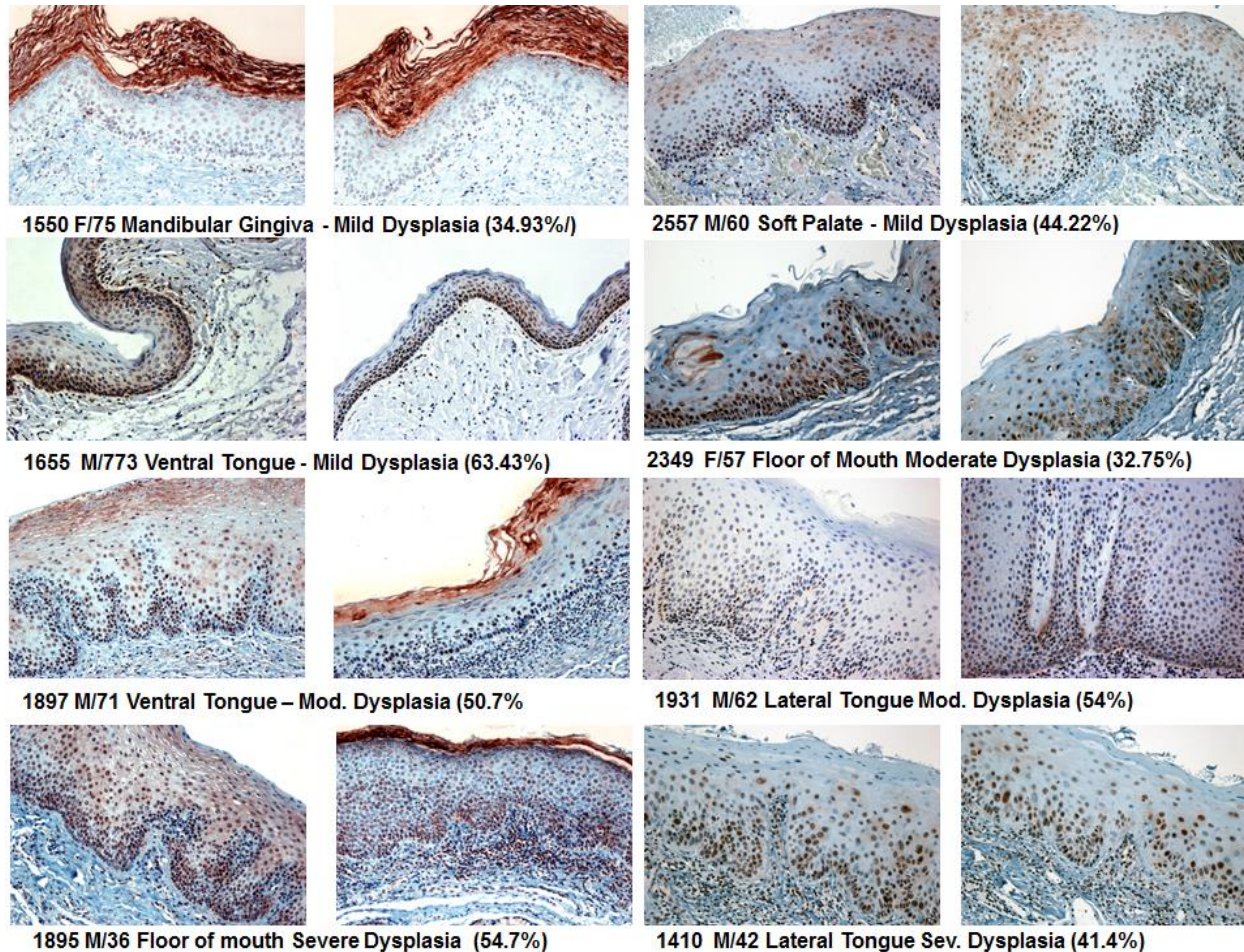


Figure 9. The RAR β expression by IHC in the extended clinical cohort showed heterogeneity confirming the presence of both mortal and immortal population of cells.