RESULTS

Cells were treated with DMSO (solvent control), 5 μM bexarotene alone (not pictured), or 5 μM pioglitazone and 0.5 μM bexarotene in combination with a differentiation mixture (insulin, dexamethasone, 3-isobutyl-1-methylxanthine) for 24 h. As expected, FABP4 and PPARγ expression levels were downregulated in both HOK-16B and MSK Leuk1 cells in a dose dependent manner. CA 9-22 cells demonstrated significant FABP4 activity with only 0.5X differentiation mix treatment (* = P<0.05, ** = P<0.01).

CONCLUSIONS

FABP4 transcriptional activation was increased by adipocyte differentiation mixture, pioglitazone, and bexarotene in both normal oral keratinocytes and leukoplakia cells. FABP4 transcriptional activation was not significantly increased in a dose dependent manner in HNSCC cells.

Combination pioglitazone and bexarotene increased FABP4 transcriptional activity in normal oral keratinocytes and leukoplakia cells. Combination FABP4 transcriptional activity was not increased in HNSCC cells. Combination treatment also did not provide an additive effect.

Cell proliferation decreased with combination treatment, significantly in normal and leukoplakia cell lines, via MTT assay. Treatment with pioglitazone and bexarotene increases lipid accumulation as demonstrated by Oil Red O staining.

We conclude the clinically relevant PPARγ activators, pioglitazone can activate FABP4 and adipocyte differentiation in normal keratinocyte cell lines and may be useful in upregulating differentiations in oral premalignant clinical trials either alone or in combination with a retinoid.