	sex	age	race	Smoking(+/-)	Drink(+/-)	Tumor location	TNM	Degree of differentiation
1	Male	63	Caucasian	+	+	tongue	T3N1M0	medium
2	Male	74	Caucasian	+	+	tongue	T2N2bM0	low
3	Male	75	Caucasian	+	+	gingiva	T2N2bM0	low
4	Male	66	Caucasian	-	+	gingiva	T2N2M0	high
5	Male	55	Caucasian	+	+	gingiva	T4N2bM0	medium
6	Male	66	Caucasian	+	+	gingiva	T4aN0M0	low

Table S1: The clinical characteristics of the patients with OSCC used in this study.
All patients were male Caucasian with age range 55-74 years, clinical TNM stages III/IV, and different hi stopathological degree of differentiation.

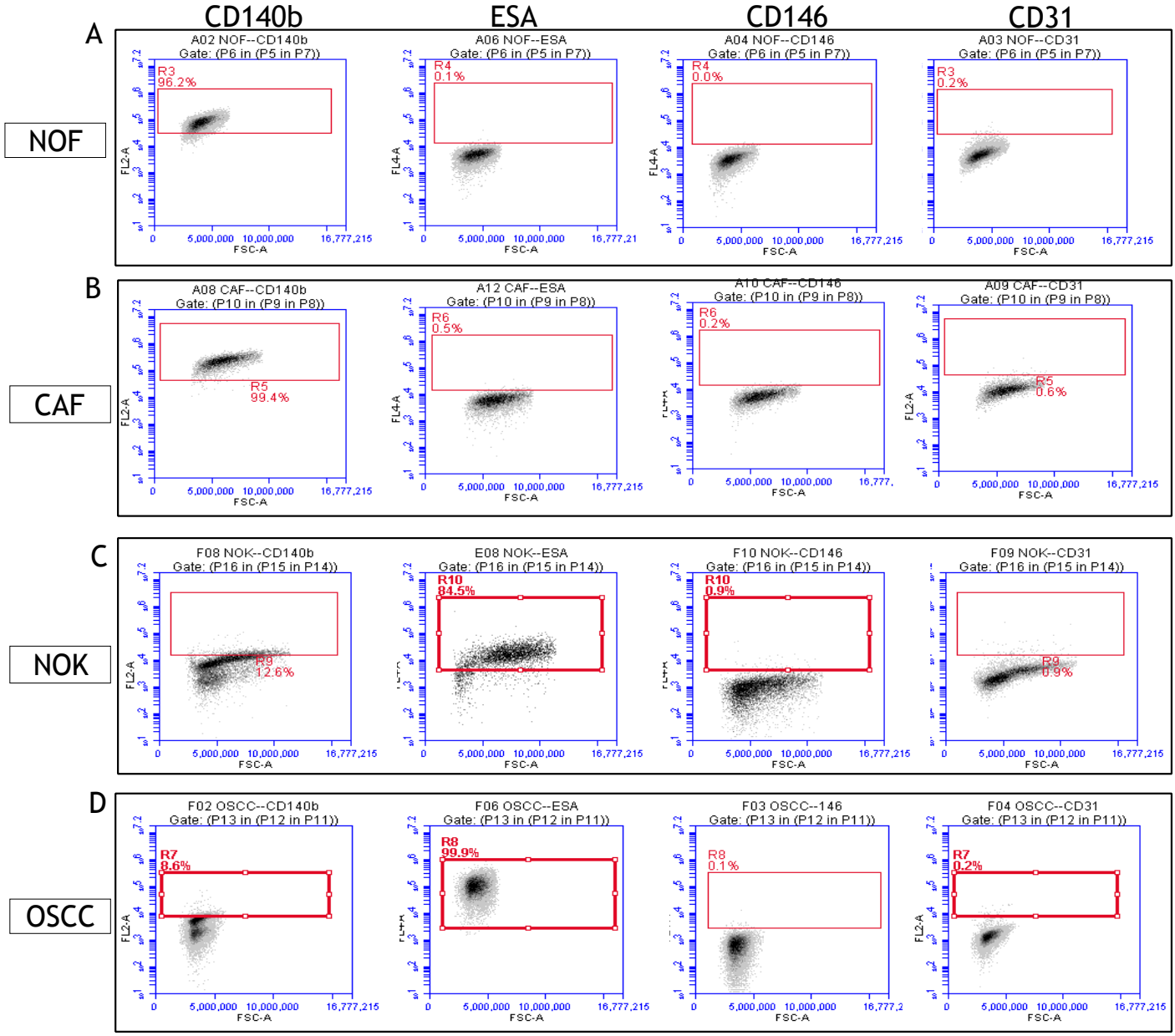


Fig S1. Flow cytometric analysis for the purity of all primary cells after generation. The purity of each strain of primary cells, NOF, CAF, NOK and OSCC was confirmed by flow cytometry which showed that 96.2% of NOFs and 99.4%of CAFs stained positively with CD140b that recognizes the platelet derived growth factor b receptor (PDGFBR), a mesenchymal lineage marker. No expression of epithelial specific antigen (ESA) - an epithelial cell marker, CD146 and CD31 - the endothelial markers was detected in neither NOFs or in CAFs. The purity of epithelial cells were 84.5% of NOKs with ESA positive cells and 99.9% for OSCCs, while 12.6% of NOKs and 8.6% of OSCCs were stained positively with CD140b. No expression of CD146 and CD31 was detected in neither NOKs or in OSCCs. We also performed the western blot to distinguish the different expression level for the mesenchymal markers α-smooth muscle actin (α-SMA).

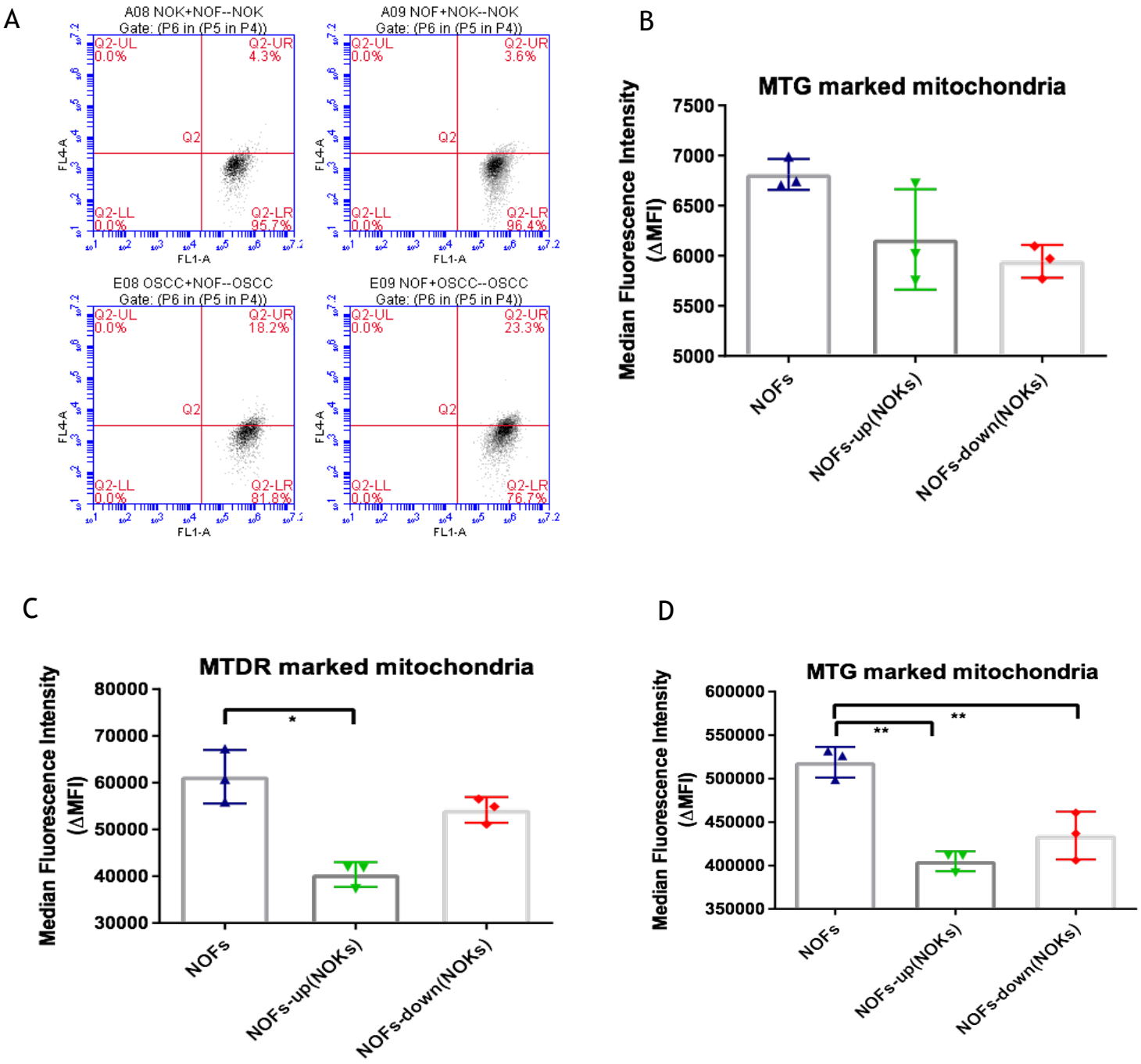


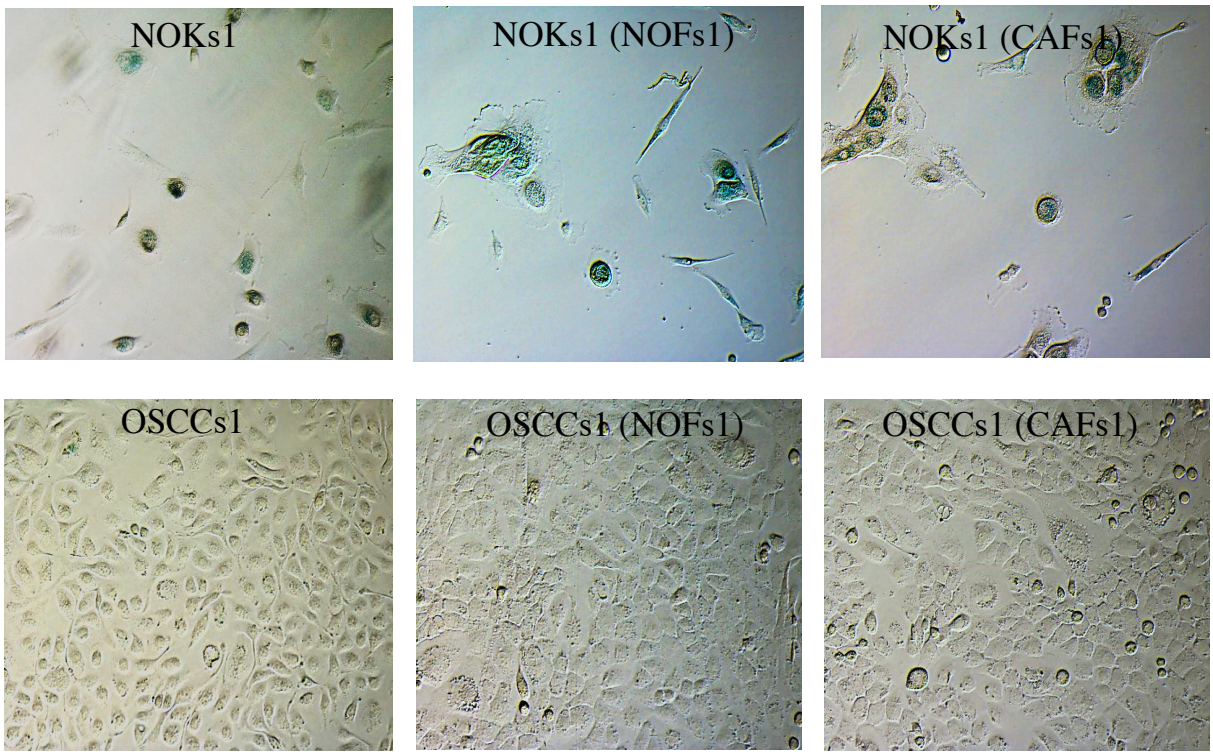
Fig S2: Indirect mitochondrial transfer from fibroblasts to OSCC in only one-direction.

A. Flow cytometry analysis quantifying the mitochondrial transfer from NOFs to OSCCs after 48h. It shows a one-direction transfer from NOFs to OSCCs, with no obvious transfer from NOFs to NOKs, or from epithelial cells to NOF, irrespective of which cell type is on top or the bottom of transwells (eliminating the gravitation as a non-specific cause for the mitochondrial transfer).

B, C, D. Quantification of the indirect mitochondrial transfer by flow cytometry between NOFs with MTDR and NOKs stained with MTG after co-cultured for 48 h in transwell. There was no significantly increasing of MTDR in NOKs after co-culture with NOFs, while slightly decreasing of MTG in NOKs can be found after co-culture.

All points represent mean values and SEM. Independent experiments were performed more than three times. * $p<0.05$; ** $p<0.01$, Paired *t* test was used.

A



B

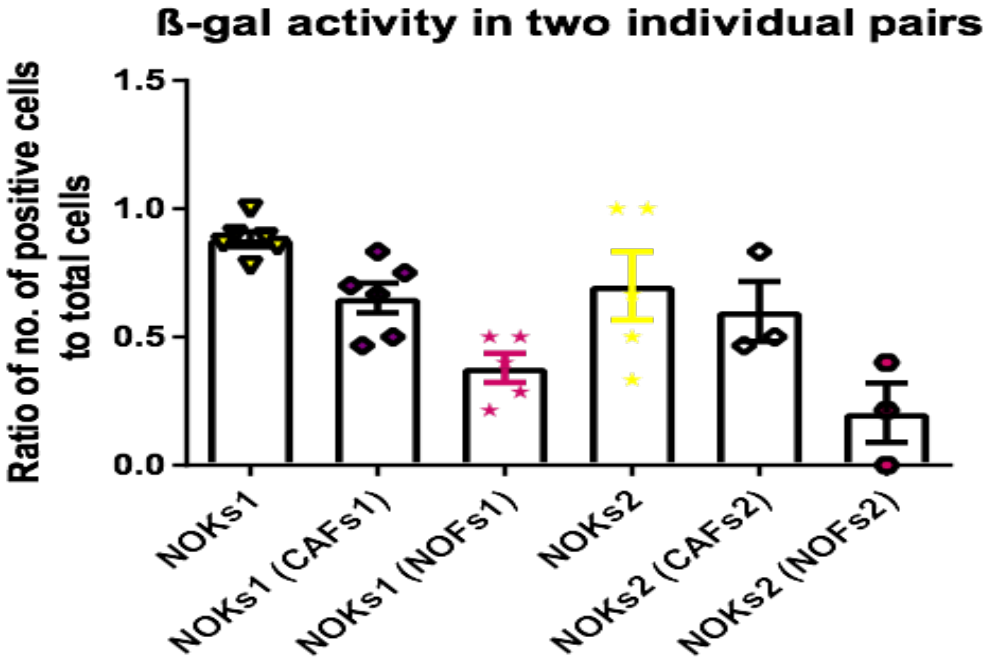


Fig S3. Assessment of senescence β-galactosidase activity for two pairs of NOKs and OSCCs alone or in co-culture.

A: Representative images for β-galactosidase staining of two pairs NOKs and OSCCs alone and co-cultured with NOFs or CAFs. All the other types of cells. (magnification 20X)

All points represent mean values and SEM. Independent experiments were performed more than three times.

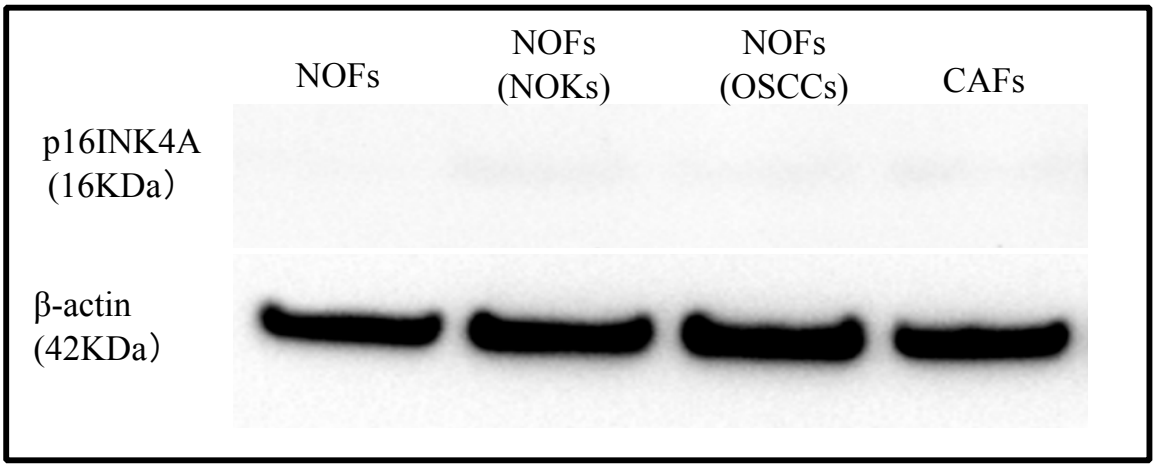


Fig S4. Western blotting with p16INK4A antibody for NOFs and CAFs alone or NOFs in co-culture

Western blotting with p16INK4A antibody demonstrated that NOFs alone, NOFs co-cultured with NOKs, NOFs co-cultured with OSCCs and CAFs alone did not show expression of p16INK4A .