

## Supplemental Materials and Methods

### DNA microarray analysis

Whole cell RNA was taken from oral keratinocytes and fibroblasts treated with 2% or 0.5% O<sub>2</sub> for 72 hr (N=1). Microarray analysis was performed by Filgen Inc. (Nagoya, Japan) with GeneChip® Human Gene 2.0 ST Array (Thermo Fisher Scientific) or Toray Industries Inc. (Tokyo, Japan) with 3D-Gene Human Oligo chip 25k. The fluorescence images of hybridized microarrays were obtained with GeneChip® scanner 3000 7G (Thermo Fisher Scientific) or 3D-Gene Scanner (Toray). Scanned data were transformed into numerical values and analyzed using Expression Console™ Software (Thermo Fisher Scientific) or 3D-Gene Extraction software (Toray). The method of Robust Multichip Array (RMA) was applied to adjust the data.

**Table S1: DNA microarray analysis**

| Gene Symbol | Gene Description                                      | EC number            | Fold Change vs normoxia |                     |                   |                     |
|-------------|---|----------------------|-------------------------|---------------------|-------------------|---------------------|
|             |   |                      | Oral Keratinocytes      |                     | Oral Fibroblasts  |                     |
|             |   |                      | 2% O <sub>2</sub>       | 0.5% O <sub>2</sub> | 2% O <sub>2</sub> | 0.5% O <sub>2</sub> |
| ASL         | argininosuccinate lyase                               | 4.3.2.1              | 0.93                    | 0.83                | 0.69              | 0.62                |
| ASS1        | argininosuccinate synthase 1                          | 6.3.4.5              | 0.57                    | 0.61                | 0.20              | 0.80                |
| GOT1        | glutamic-oxaloacetic transaminase 1                   | 2.6.1.1              | 0.83                    | 0.82                | 0.65              | 0.71                |
| GOT2        | glutamic-oxaloacetic transaminase 2                   | 2.6.1.7              | 1.06                    | 0.93                | not detected      |                     |
| GPI         | glucose 6-phosphate isomerase                         | 5.3.1.9              | 1.25                    | 1.38                | 1.50              | 1.71                |
| ODC1        | ornithine decarboxylase                               | 4.1.1.17             | 0.49                    | 0.49                | 0.16              | 0.17                |
| PFKFB3      | 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 | 2.7.1.105 / 3.1.3.46 | 1.47                    | 2.74                | 3.36              | 2.29                |
| PGD         | 6-phosphogluconate dehydratase                        | 4.2.1.12             | 1.04                    | 1.11                | 0.86              | 1.09                |
| PRPS1       | phosphoribosyl pyrophosphate synthetase1              | 2.7.6.1              | 0.74                    | 0.64                | 0.48              | 0.63                |
| PRPS2       | phosphoribosyl pyrophosphate synthetase2              | 2.7.6.1              | 0.75                    | 0.75                | 0.94              | 1.13                |
| RPIA        | ribose 5-phosphate isomerase A                        | 5.3.1.6              | 0.77                    | 0.71                | 0.88              | 0.87                |
| TALDO1      | transaldolase1  | 2.2.1.2              | 0.97                    | 0.97                | 0.45              | 0.60                |

Gene expression changes of enzymes in PPP and urea cycle (N=1). Relative gene expression of 2% O<sub>2</sub> or 0.5% O<sub>2</sub> vs normoxia of oral keratinocytes and fibroblasts are shown.