

# **The cutaneous beta human papillomavirus type 8 E6 protein induces CCL2 through the CEBP $\alpha$ /miR-203/p63 pathway to support an inflammatory microenvironment in epidermodysplasia verruciformis skin lesions**

**Luca Vella<sup>1</sup>, Anna Sternjakob<sup>1</sup>, Stefan Lohse<sup>1</sup>, Alina Fingerle<sup>1</sup>, Tanya Sperling<sup>2</sup>, Claudia Wickenhauser<sup>3</sup>, Michael Stöckle<sup>4</sup>, Thomas Vogt<sup>5</sup>, Klaus Roemer<sup>6</sup>, Monika Oldak<sup>1,7</sup>, Sigrun Smola<sup>1,8\*</sup>**

<sup>1</sup>Institute of Virology, Saarland University Medical Center, Homburg/Saar, Germany

<sup>2</sup>Institute of Virology, University of Cologne, Cologne, Germany

<sup>3</sup>Institute of Pathology, University of Cologne, Cologne, Germany

<sup>4</sup>Department of Urology and Pediatric Urology, Saarland University Medical Center, Homburg/Saar, Germany

<sup>5</sup>Department of Dermatology, Saarland University Medical Center, Homburg/Saar, Germany

<sup>6</sup>Jose Carreras Center for Immune and Gene therapy, Saarland University Medical Center, Homburg/Saar, Germany

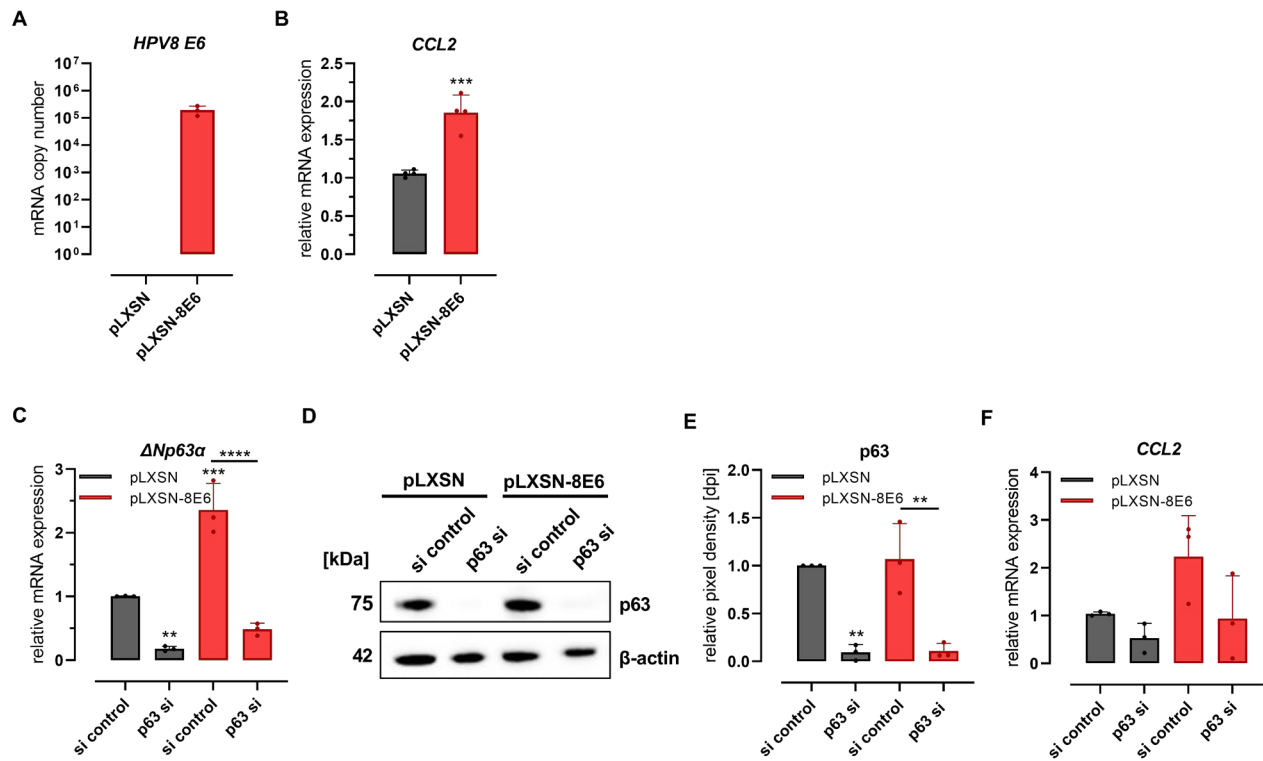
<sup>7</sup>Department of Histology and Embryology, Medical University of Warsaw, Warsaw, Poland

<sup>8</sup>Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Helmholtz Centre for Infection Research, Saarbrücken, Germany

**\* Correspondence:**

Sigrun Smola

sigrun.smola@uks.eu



**Figure S3: HPV8 E6 mediates CCL2 induction in NHK:** (A-B) NHK were retrovirally engineered to express HPV8 E6 (red) or empty pLXSN vector (gray). Expression of HPV8 E6 (A) and CCL2 (B) mRNAs was determined by qRT-PCR. (C-F) NHK were treated with siRNA targeting p63 or control siRNA (si). Expression of  $\Delta Np63\alpha$  mRNA was detected by qRT-PCR (C), of total p63 protein by immunoblot (D, representative images, E, densitometry of three independent experiments), and of CCL2 mRNA by qRT-PCR (F). Results of qRT-PCR are demonstrated as “relative mRNA expression” normalized to RPL13a housekeeping gene expression and as “relative pixel density [dpi]” normalized to  $\beta$ -actin calculated by imageJ. Significant difference were calculated with two-tailed unpaired t-test (A-B) and two-way Anova and Sidak correction (C-F) for multiple comparison and displayed as \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  and \*\*\*\*  $p < 0.0001$ .