*In silico* analysis reveals EP300 as a panCancer inhibitor of anti-tumor immune response via metabolic modulation.

Rosemarie Krupar<sup>1,2,+,\*</sup>; Christian Watermann<sup>1,+</sup>; Christian Idel<sup>3</sup>; Julika Ribbat-Idel<sup>2</sup>; Anne Offermann<sup>2</sup>; Helen Pasternack<sup>2</sup>; Jutta Kirfel<sup>2</sup>; Andrew G. Sikora<sup>4</sup>, Sven Perner<sup>1,2</sup>

<sup>1</sup>Research Center Borstel, Leibniz Lung Center, Borstel, Germany

<sup>2</sup>Pathology of the University Hospital Schleswig-Holstein, Campus Luebeck, Germany

<sup>3</sup>Department of Otorhinolaryngology, University Hospital Schleswig-Holstein, Luebeck, Germany

<sup>4</sup>Department of Otorhinolarygology – Head and Neck Surgery, Baylor College of Medicine, Houston, USA

<sup>+</sup>These authors contributed equally to the work

\***Corresponding author:** Rosemarie Krupar, Research Center Borstel, Leibniz Lung Center, Parkallee 3A, 23845, Borstel, Germany, Email: <u>rkrupar@fz-borstel.de</u>, Phone: +49-4537-188-6290, Fax: +49-04537-188-2290

**Supplementary figures** 

## Suppl. figure 1



## Suppl. figure 2





## Figure legend supplementary figures:

**Suppl. figure 1:** Association of EP300 expression and mutation status with the tumor immune landscape across **18 solid malignancies.** The distribution of the six immune profiles (C1 – C6), defined by Thorsson *et al.*, were compared between tumors with *EP300* wt and *EP300* mut status as well as EP300 high and low expression. The Interferon-γ dominant immune subtype C2 was significantly more frequent in *EP300* mut and EP300 low tumors. In contrast the inflammatory subtype C3 was more often found in *EP300* wt and EP300 high expressing tumors. Additionally EP300 low tumors had a higher number of C4 subtypes (lymphocyte depleted). C1: wound-healing, C2: Interferon-γ dominant, C3: inflammatory, C4: lymphocyte depleted, C5: immunologically quiet, C6: TGF-β dominant. wt: wildtype; mut: mutated; Mut: Mutation; Expr.: Expression; ns: not significant. \*: p<0.05, \*\*: p<0.01, \*\*\*: P<0.001, \*\*\*\*: p<0.0001.

**Suppl. figure 2: PanCancer analyses of metabolic phenotypes in relationship to** *EP300* **mutation status: A**) Upregulation frequency relative to number of analyzed tumors for *EP300* wt (n=4694) and *EP300* mut (n=233) displaying 24 genes involved in glycolysis and 31 genes involved in OXPHOS. **B**) Relative upregulation frequency of glycolysis- and OXPHOS-associated genes with a subtle, but significant higher glycolysis- and OXPHOS-dependent metabolism in *EP300* mut tumors. \*: p<0.05, \*\*: p<0.01, \*\*\*: P<0.001, \*\*\*\*: p<0.001.