

## ***Supporting Information***

### **Cetuximab prevents methotrexate-induced cytotoxicity *in vitro*, through epidermal growth factor dependent regulation of renal drug transporters**

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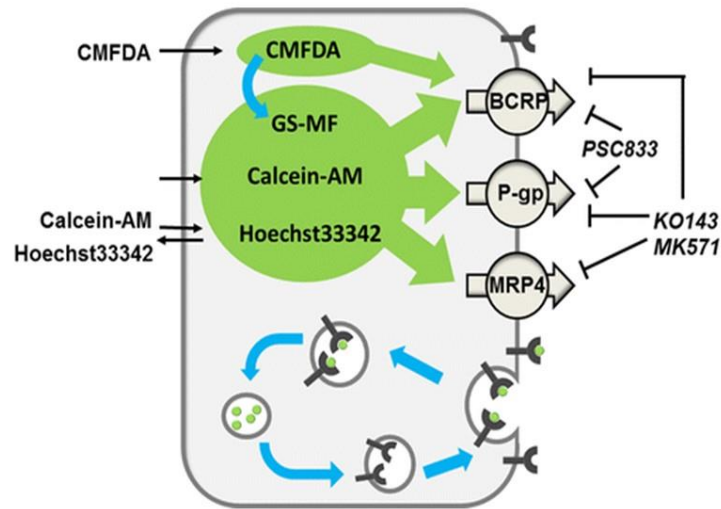
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**Table S1:** *ciPTEC culture medium formulation*

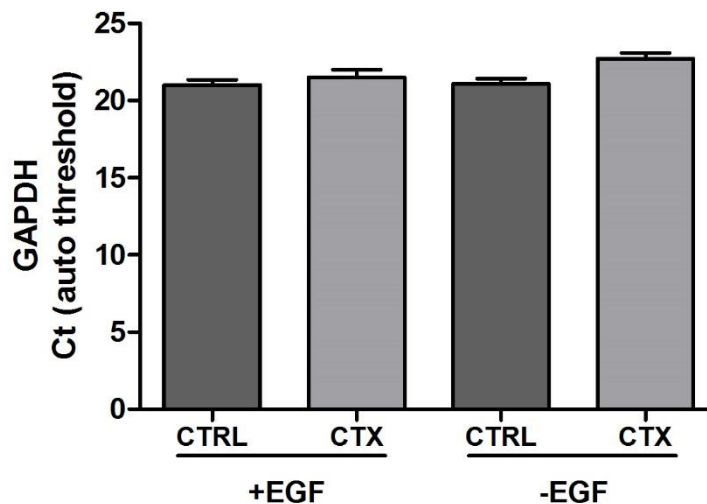
		Distributor	Concentration
<b>Medium</b>	DMEM-F12	Thermo Fisher-	-
	HEPES, no phenol red	Gibco	-
	Insulin	Sigma-Aldrich	5µg/ml
	Transferrin	Sigma-Aldrich	5µg/ml
	Sodium	Sigma-Aldrich	5ng/ml
<b>Supplements</b>	Hydrocortisone	Sigma-Aldrich	36ng/ml
	Epidermal growth factor	Sigma-Aldrich	10ng/ml
	Tri-iodothyronine	Sigma-Aldrich	40pg/ml
	FCS	Greiner Bio-one	10% (v/v)

**Table S2:** *Pathways identified as significant matches to the kinase phosphorylation sites obtained from the PTK/STK PamChip® array. The list of pathways was obtained based on statistical analysis of the phosphorylation targets and overlap with pathway targets retrieved from associated databases. Pathways with  $-\log(pvalue)$  above 4 were considered significant. Conditions: +EGF (orange); +EGF+CTX (blue); +CTX (red)*

#	Maps	0	2	4	6	$-\log(pvalue)$
1	Development c-Kit ligand signaling pathway during hemopoiesis	0.5	1.5	3.5	6.5	6.5
2	Development growth factors in regulation of oligodendrocyte precursor cell proliferation	0.5	1.5	3.5	6.5	6.5
3	Immune response inhibitory PD-1 signaling in T-cells	0.5	1.5	3.5	6.5	6.5
4	Role of $\alpha$ -6/ $\beta$ -4 integrins in carcinoma progression	0.5	1.5	3.5	6.5	6.5
5	Signal transduction PKA signaling	0.5	1.5	3.5	6.5	6.5
6	Oxidative stress activation of NADPH	0.5	1.5	3.5	6.5	6.5
7	Development EGFR signaling pathway	0.5	1.5	3.5	6.5	6.5
8	Development gastrin in cell growth and proliferation	0.5	1.5	3.5	6.5	6.5
9	Main growth factor signaling cascades in multiple myeloma cells	0.5	1.5	3.5	6.5	6.5
10	Development VEGF signaling via VEGFR2 – generic cascades	0.5	1.5	3.5	6.5	6.5



**Figure S1:** Graphic abstract of "Fluorescence-Based Transport Assays Revisited in a Human Renal Proximal Tubule Cell Line". The interactions of several fluorescent substrates and model inhibitors with the major apical drug transporters present in proximal tubule epithelial cells.



**Figure S2:** Cycle threshold (Ct) values for GAPDH in the different experimental conditions used in the present study. GAPDH expression was stable and no statistically significant differences were observed between the different treatments.

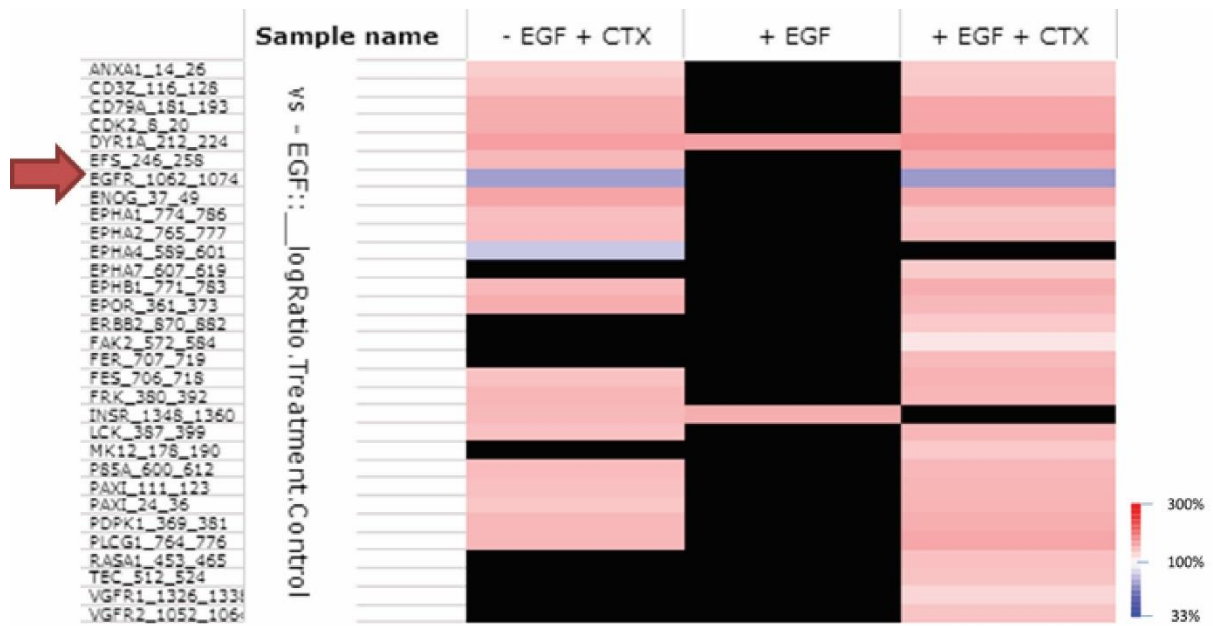


Figure S3: Cetuximab inhibition of the EGFR phosphosite.

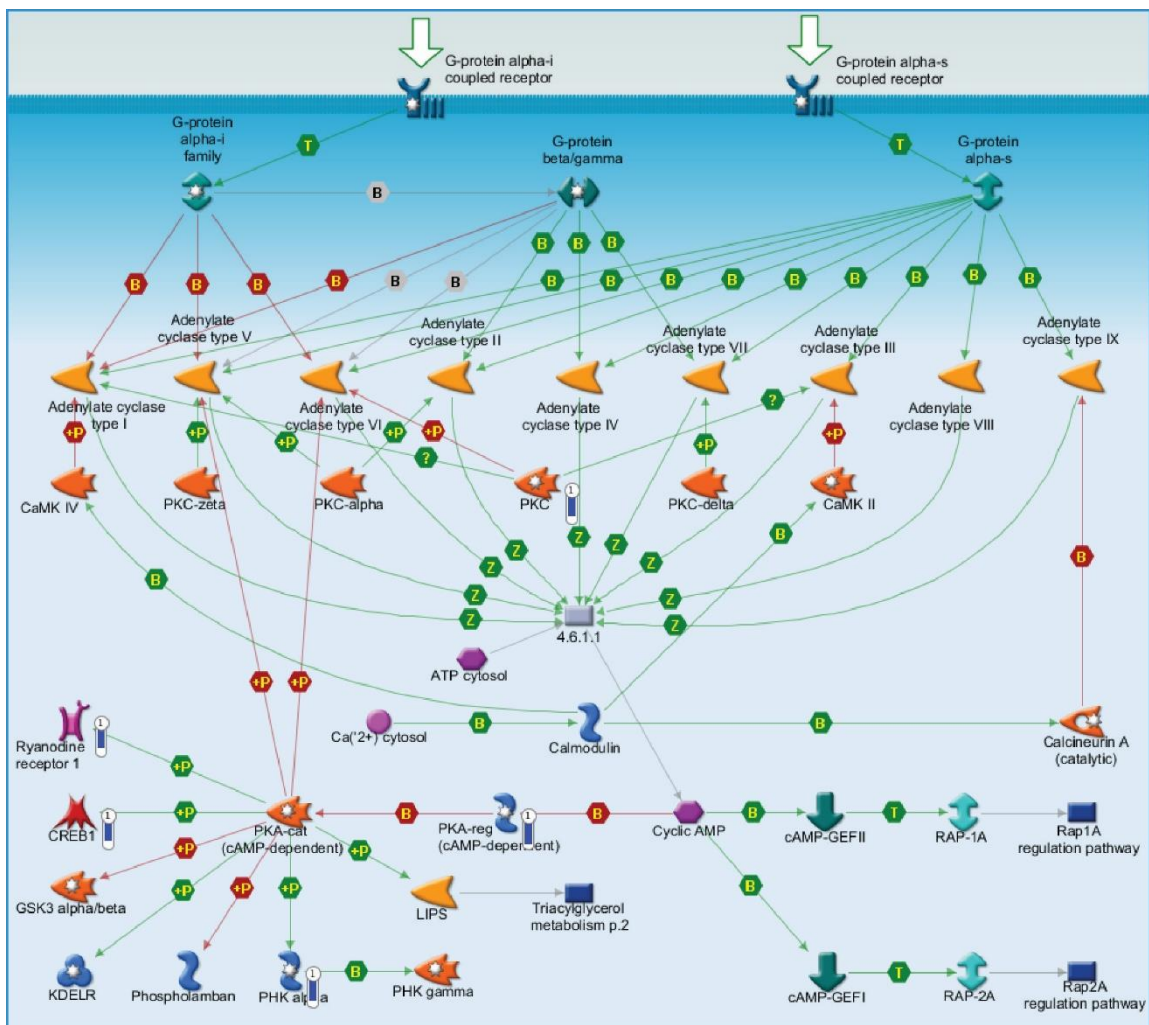
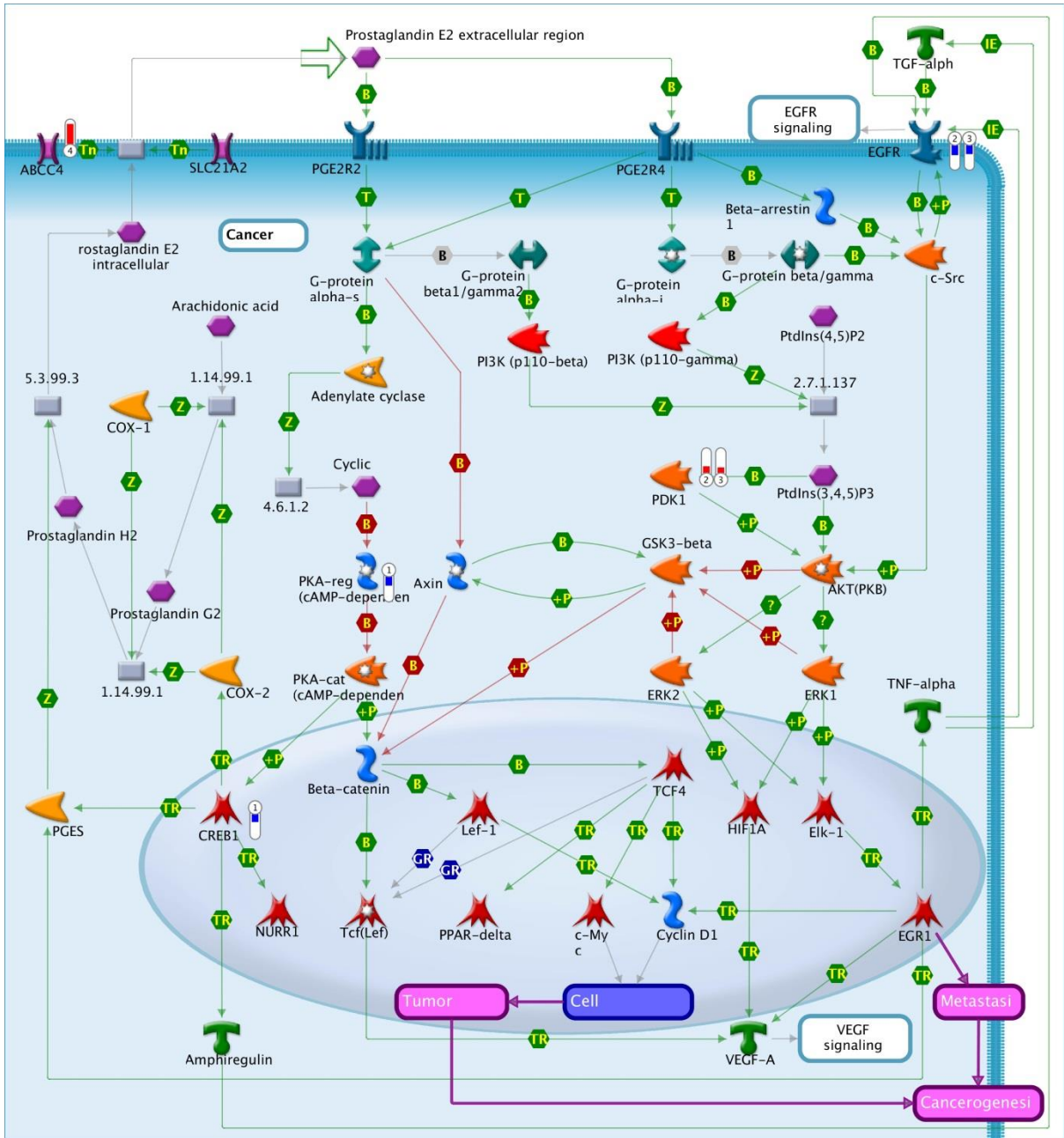
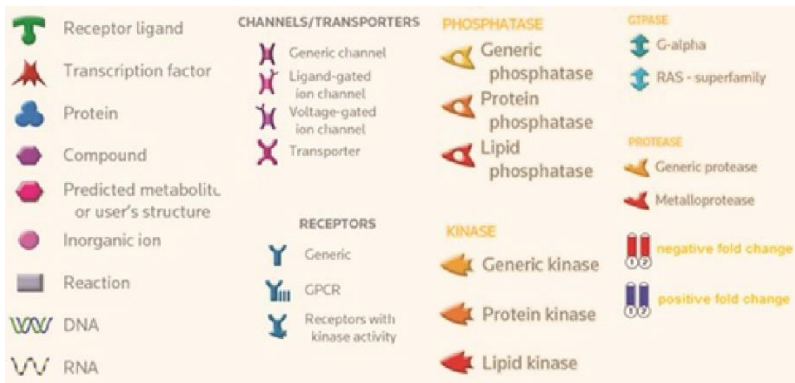


Figure S4: Metacore knowledge-based pathway analysis of the effect of EGF (control condition) on ciPTEC-OAT1



**Figure S5:** Metacore knowledge-based pathway analysis of the effect of EGF together with Cetuximab on ciPTEC-OAT1.



**Figure S6:** Pathway analysis symbols key