ACH-1.10 Glucose restriction increases the antiproliferative response of colorectal carcinoma (CRC) cells to 5-fluorouracil (5FU) (W)

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Background
Chemotherapy is still essential in anti-cancer therapies, but linked to harmful side effects. Starvation conditions can sensitize cancer cells to drugs in contrast to healthy cells Clinical studies have shown that short-term starvation before/after chemotherapy protects from side effects. Since cancer cells show high glycolytic activity we analyzed the impact of glucose restriction on the antiproliferative response of CRC cells to 5FU.

Methods
Human CRC cell lines (Colo741, LS174T, HCT116, HT29, SW620) and nonmalignant fibroblasts were cultured with 11mmol/l glucose (nonstarved condition) or 2.7mmol/l glucose (a concentration that humans can reach after fasting) and exposed to 5% oxygen (O2), representative for tumor microenvironment. Cell response to 5FU was determined by calculating the half-maximal inhibitory concentration (IC50) after 72h.

Results
Glucose starved CRC cells demonstrated an increased antiproliferative response to 5FU and cell proliferation retarded. Three cell lines were clearly sensitized to 5FU shown by decreased IC50 values up to 4-fold (p<0.05) in comparison to nonstarved cells. In contrast, glucose starvation protected fibroblasts against the antiproliferative effect of 5FU.

Conclusions
Glucose restriction can specifically sensitize CRC cells to 5FU. The fact that this sensitization was observed at 5% O2 (in contrast to 21% & 1% oxygen), representative to tumor microenvironment, underline the importance of this parameter for further analyzes of the mechanisms of glucose starvation in sensitizing CRC cells to 5FU.