

#### Additional file 4: Calculations of cost of tumor based on glucose utilization

$p_{cancer}$  is calculated using equation (21) in the main text.

To calculate the estimated cost of the tumor based on glucose turnover and glucose recycling,  $P_{cost\_glucose}$ , equations (22) in the main text are used to calculate  $p_{anaerobic}$ . This assumes that the increased glucose turnover enters the cancer, and that the increased Cori cycling is due to glucose being recycled as a result of the glucose being metabolized anaerobically by the tumor.  $p_{anaerobic}$  is equivalent to  $X_{anaerobic}$  using the following formula (assuming glucose is used for either aerobic or anaerobic energy)

$$X_{anaerobic} = p_{anaerobic} / (p_{anaerobic} + 15(1 - p_{anaerobic})) \quad (1)$$

The increased glucose turnover in g/kg patient/day is converted to increased mol glucose/kg patient/day using the molecular mass of glucose, 180.16 g/mol, to get mol glucose/kg patient/day increase. Based on  $X_{anaerobic}$ , the amount of glucose used anaerobically by the tumor is calculated. This leads to mol glucose/kg patient/day recycled in the Cori cycle. 6 mol ATP is needed per mol glucose/kg/day recycled, leading to mol ATP/kg/day Cori cycling cost. Assuming the liver generated its energy aerobically, we use 30 mol ATP/mol glucose consumed by the liver, to get a mol glucose consumed by liver/kg/day Cori cycle cost. We convert this to g glucose consumed by liver/kg/day for Cori cycle, using again 180.16 g/mol molecular weight of glucose. Then we convert this value to kcal/kg/day using the conversion parameter of 4.2 kcal/g used by Hall [1] to get the Cori cycle cost in kcal/kg/day. As seen in Table S1, the value of  $X_{anaerobic}$  leads to the percentage the Cori cycle cost is of the total cost of the cancer. The total cost of the cancer is then calculated in kcal/kg patient/day. In Table 2, the cost,  $P_{cost\_glucose}$ , is then displayed for a 70kg patient.

In study B, where an estimate of the tumor burden is available, we are able to use the same method to calculate the specific cost of cancer,  $K_{cost}$ , for a 70kg patient, with the assumption of  $X_{anaerobic}=25\%$ .

#### References

1. Hall KD: **Computational model of in vivo human energy metabolism during semistarvation and refeeding.** *Am J Physiol Endocrinol Metab* 2006, **291**:E23-E37.