Supplementary Material

1 DERIVATIONS OF SCALING RELATIONSHIPS AND GROWTH EQUATIONS

1.1 Derivation of scaling between metabolic and gross tumor volume

A final extension of metabolic scaling theory is the prediction of a scaling relationship between metabolic tumor volume (MTV) and gross tumor volume (GTV). The region of the tumor excreting angiogenic factors and performing vessel recruitment is assumed to exist near the tumor boundary and have a thickness τ determined by the diffusion distance. Assuming the tumor has attached to vessels in the L^{th} generation of the surrounding vascular network, the rate blood flow to the tumor, $\dot{Q}_T$, is the sum of all L^{th} generation host vessels with blood flow rates $\dot{Q}_L$ intersecting the tumor boundary, and expressed as $\dot{Q}_T = \rho_L S_T \tau \dot{Q}_L$, where S_T is the total tumor surface area and ρ_L is the number density of L^{th} generation vessels within the host body. This number density is defined as the number of all L^{th} generation vessels divided by the total host body volume $\rho_L = N_L/V$. Substituting for ρ_L, and the surface area to volume scaling relationship $S_T \propto V_T^{2/3}$, gives $\dot{Q}_T \propto V_T^{2/3} \tau N_L \dot{Q}_L / V$.

Here we call on several results of metabolic scaling theory. First is the linear scaling relationship between organ or organism volume and mass, resulting in $\dot{Q}_T \propto m_T^{2/3} \tau N_L \dot{Q}_L / M$. Next we utilize fluid conservation across the branching generations in the host to equate, $N_L \dot{Q}_L = N_{cap} \dot{Q}_{cap}$. Assuming that the capillary flow rate is proportional to the metabolism of the distal cells, we make the important substitution that $N_{cap} \dot{Q}_{cap} \propto N_{cap} B_{cap}$, or simply $N_L \dot{Q}_L \propto M^{3/4}$, resulting in $\dot{Q}_T \propto m_T^{2/3} \tau / M^{1/4}$. As the diffusion distance τ is assumed to vary inversely with capillary density ρ_{cap}, then $\tau \propto V/N_{cap}$, or $\tau \propto M^{1/4}$, giving $\dot{Q}_T \propto m_T^{2/3}$. We can equate tumor blood flow rate with tumor metabolism using the same conservation of fluid argument that equated host blood flow rate with metabolism to write $B_T \propto m_T^{2/3}$. Substituting the predicted scaling relationship, $B_T \propto m_B^{\theta}$, between total tumor metabolism, B_T, and the mass of metabolically active tumor tissue, m_B, we arrive at the following scaling relationship,

$$m_B^{\theta} = m_0 m_T^{\frac{2}{3}} \tag{S1}$$

where m_0 is a normalization constant. Lastly, the linear scaling between tissue volume and mass is used to substitute metabolic tumor volume for mass of metabolically active tumor tissue ($MTV \propto m_B$) and gross tumor volume for total tumor mass ($GTV \propto m_T$) to arrive at,

$$MTV = V_0 GTV^{\frac{2}{3\theta}} \tag{S2}$$

1.2 Derivation of energetic tumor growth equation

Here we summarize the main points of growth and development models from the context of metabolic scaling theory, in particular as it relates to tumors West et al. (2001); Herman et al. (2011); Guiot et al. (2006). Although the data considered in this study consists entirely of single point-in-time measurements, this formalism still provides informative insight and interpretations of metabolic scaling for the potential of

tumor detection and growth forecasting. We begin with the assumption that all tissue, organ, or organism metabolism, B_{tot}, can be divided between the processes of growth and maintenance as,

$$B_{tot} = E_c \frac{dm}{dt} + B_c m \tag{S3}$$

where E_c is the energetic cost of growth, m the mass of cells present at time t, and B_c the metabolic cost of maintenance. Substituting Kleiber's law for total metabolism, $B_{tot} = B_0 m^\theta$, this statement can be re-written as an ordinary differential equation for growth as,

$$\frac{dm}{dt} = \alpha m^\theta - \rho m \tag{S4}$$

where $\alpha = B_0 m_c / E_c$ and $\rho = B_c / E_c$. Eq. (S4) is also known as the von Bertalanffy growth model Von Bertalanffy (1957).

Within this regime the asymptotic mass can be substituted for $\alpha = \rho / m_{eq}^{1-\theta}$. Defining $\widetilde{m} = m/m_{eq}$ non-dimensionalizes Eq. (S4), resulting in,

$$\frac{d\widetilde{m}}{dt} = \rho \widetilde{m}^\theta - \rho \widetilde{m} \tag{S5}$$

where ρ can now be seen to serve effectively as a proliferation rate.

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