Supplemental information

Diffusion calculations

Interferons and other antiviral cytokines are smaller than virus particles, so they are able to diffuse more rapidly through semi-solid gels or liquid media. Cytokines and virus particles are also produced by cells with characteristic time-delays which may be estimated from experiments. When processes of diffusion and production are coupled, cytokines or viruses can spread spatially. For spreading infections, Ortega-Cejas et al. (Ortega-Cejas et al., 2004) have derived an approximate expression for the speed of the spread:

$$V = \sqrt{\frac{2 \cdot \mathcal{D}_{eff}}{\tau}}$$

where $\mathcal{D}_{eff}$ is the effective diffusivity of the virus and τ is the delay time that is characteristic of the virus production. Our data suggest the time delay τ for virus replication and cytokine production to be approximately 3 hours and 4 hours, respectively. Further, the Stokes-Einstein equation can be adapted to estimate the diffusivity of a solute (cytokine):

$$\mathcal{D}_{eff} = \frac{\kappa T}{6\pi R_h \mu_B}.$$

where κ is Boltzmann's constant, T is temperature, and μ_B is the viscosity of the bulk fluid and R_h is the Stokes, or hydraulic, radius of the particle. We use published data to estimate $\mathcal{D}_{eff}$. This allowed us to estimate the diffusion speeds of antivirals and virus in a 0.6% agarose gel as used experimentally, shown in Table 1.

Table 1: Diffusion calculations for virus (upper table) and antiviral molecules (lower table) in media and in 0.6% agar gels.

	Particle shape/size (nm)	Diffusivity (um^2/sec)	Source
T4 phage in 1% agar	80x100 nm + 120 nm long tail	1.9	Experimentally determined (Hu et al., 2010)
Nanobeads in 0.6% agar	Spherical beads 100 nm in diameter	~0.75	Experimentally determined in 0-3% agarose gels. (Yakimovich et al., 2012)
	Particle shape/size (nm)	**Diffusivity (um^2/sec)**	**Source**
IFN in water/agar*	IFNα: MW = 19.2 kDa R_h = 2.12 nm (Grace et al., 2005) IFNβ: MW = 18.5 kDa	158.8	Stokes-Einstein for sphere of radius 2.12 nm in water at 37°C.
Lactalbumin in water/agar*	Lactalbumin: MW = 14.2 kDa R_h = 1.90-2.12 nm (Pluen et al., 1999)	114-130	Experimentally determined (Saltzman et al., 1994) (Pluen et al., 1999)

*At a hydraulic radius of 2.12 nm, there should be little impedance of diffusion due to agar gels or other matrices with similar pore size, including biologically-derived matrices such as human cervical mucus (Pluen et al., 1999; Saltzman et al., 1994). Thus the diffusivity of interferon in water should be similar to that in agar.

**the width of one A549 cell is approximately 12 μm (Jiang et al., 2010).

Supplemental References

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