Modeling of parvovirus treatment of cancer

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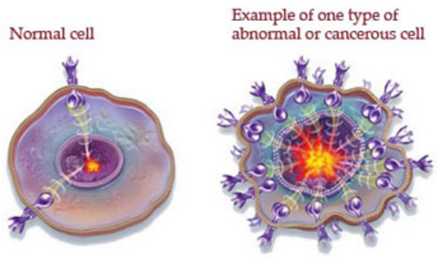
Abstract

Rat Parvovirus is found in rat liver and can infect and cause changes in tumor cells. When tumor cells are infected, the cells can revert back to benign or uncancerous cells. We describe and analyze a mathematical model of infected and noninfected tumor cells when introduced to the parvovirus. We examine model predictions of tumor cure as the fraction of reverted cells is changed.

Motivation

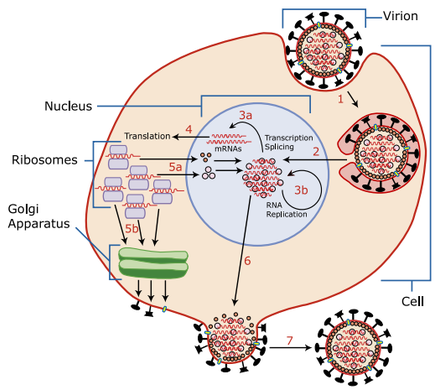
- Current cancer treatments can have serious side effects, so new treatments are being explored.
- Viruses that can kill tumor cells without causing general infections in patients are a promising possible treatment.
- Here we explore whether a virus that changes cancer cells to a non-cancerous or benign cell can be used as treatment.
- We use a mathematical model to analyse how tumor treatment responds to changes in a viruses ability to cause reversion.

Cancer



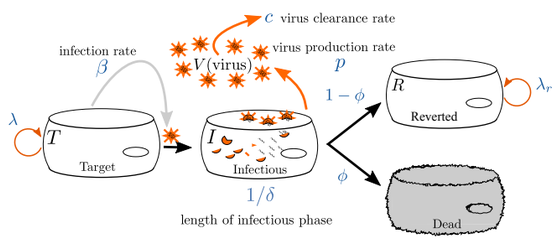
- Cancer is caused by cells that have mutated, losing the ability to function properly and limit replication.
- Common treatments are chemotherapy, radiation, or surgery which all have serious side effects.

Viral replication



Viruses infect cells by binding to surface proteins and fusing with the cell membrane. Once inside, the virus uses the cell's replication machinery to make copies of itself.

Mathematical model



- Virus replicates by infecting tumor target cells.
- Model includes the target cells, infectious cells, reverted cells, and the virus.
- Once infected, cells can die from the infection or be reverted to a benign phenotype.
- The fraction that is reverted is determined by the parameter ϕ.

$$\begin{aligned}
\dot{T} &= \lambda T\left(1-\frac{T+I+R}{K}\right)-\beta TV\\
\dot{I} &= \beta TV-\delta\phi I-(I-\phi)\delta I\\
\dot{R} &= \lambda_r R\left(1-\frac{T+I+R}{K}\right)+(1-\phi)\delta I\\
\dot{V} &= pI-cV
\end{aligned}$$

Mathematical Analysis

We found four fixed points:

- The virus kills all the cells, and the virus itself also goes to zero.

$$(T\to 0, I\to 0, R\to 0, V\to 0)$$

- A series of fixed points with a mix of reverted and target cells.

$$(T\to K-R, I\to 0, V\to 0)$$

- One fixed point results in all cells reverted and the tumor and virus are gone.

$$(T\to 0, I\to 0, R\to K, V\to 0)$$

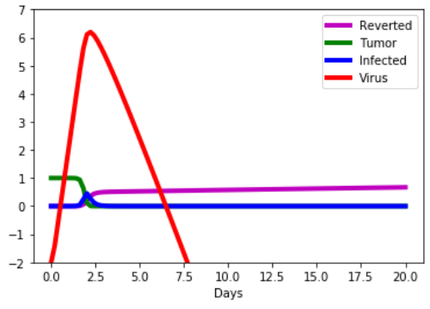
- Chronic infection can also occur where the virus, reverted cells, target cells, and infected cells are all at specific values.

$$\left(T\to\frac{c\delta(c\lambda+\beta Kp)}{\beta p(c\lambda+\beta Kp)}, I\to\frac{c\lambda[c\delta(\lambda_r+\phi\lambda-\lambda)-\beta K\lambda_r p]}{\beta\lambda_r p(c\lambda+\beta Kp)},\right.$$
$$\left.R\to\frac{c\delta\lambda(\phi-1)}{\beta\lambda_r p}, V\to\frac{c\delta(\lambda_2-\phi\lambda^2-\lambda_r)+\beta K\lambda_r p}{\beta\lambda_r(c\lambda+\beta Kp)}\right)$$

Model simulation

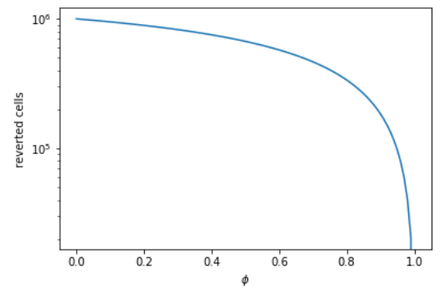
Parameter	Value
λ	0.045 /d
K	1.0×10^6
β	1.0×10^{-5} /d
δ	4.0 /d
λ_r	0.040 /d
p	20 /d
c	4.0 /d

This is a simulation of the reverted cells, tumor cells, infected cells, and the virus at specific parameters over period of time.



We find that the virus and infected cells die off, leaving some combination of reverted and tumor cells.

Effect of the fraction reverted



This is a graph of the reverted cells vs ϕ , showing the change in reverted cells at the end of the simulation as the fraction reverted changes.

Conclusions

- Our model shows distinct behaviors as the parameters change the number of reverted cells.
- If only a small fraction of cells become benign, we are still left with mostly reverted cells.

Future Directions

- There is experimental data that can be extracted and fitted to the model to get realistic parameters for parvovirus.
- We will analyze the stability of the fixed points to determine likely outcomes.
- We can investigate a stochastic version of the model to get a more realistic assessment of treatment outcomes.

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Using a virus, like the rat parvovirus, to treat cancer is a less damaging way than chemotherapy, radiation, and surgery which are the current treatments for cancer. This model is helping us understand how a virus can treat cancer and if it is an effective treatment. Our model shows that you can have a small fraction of reverted cells, but save a lot of cells.