The Flu That Cured Cancer

Luka Vukovic
November 2018

It's that time of year again. The blankets are out, tea steeping, Kleenex box ready. I'm sweating, but it's still so cold. Why did this have to happen; the coughs, muscle aches, headaches, weakness, and fever? Well, nature doesn't care and you forgot to get the flu shot again.

This is what a virus can do. It is as simple as small bubble of protein with genetic information inside, either DNA or RNA, that dictates how to use your body as a means to spread and reproduce. A virus is essentially just a code of information that eloquently explains to your cells how to make more virus until the cell dies. Viruses aren't alive, so you can actually kill a virus. With time, your body figures a way to stop it from spreading and damaging your tissues.

Now how could we possibly use these pestering infective agents to cure cancer?

Since there are so many viruses that target so many specific hosts, why not find a virus that specifically targets cancer cells? This was the reasoning behind the development of oncolytic viruses (OV), "a promising treatment modality that offers unique opportunities for tumour targeting" (Singh et al., 2012). *Onco* refers to tumor and *lytic* refers to causing lysis, or cell rupture. So how do OVs treat cancer without also giving patients a dose of the flu?

OVs distinguish between normal and cancerous cells based on their physiologies. For example, OVs can be designed to target translation of proteins. If a virus forces a cell to translate proteins: the cell, cancerous or not, will continue to make protein for the virus capsid and until eventual lysis. In specifically modified viruses for cancer treatment, the gene that forces a cell to manufacture viral protein is knocked out. As a result, normal and healthy infected cells can use cellular mechanisms to stop producing viral protein while cancerous cells; who's physiology is broken; will continue, ultimately leading to their cell death (Sarinella et al., 2006).

Another method may be to transfer the tumor suppressor gene, p53, to cancerous cells which will then recognize their broken state and undergo apoptosis, controlled cell suicide (Candelaria et al., 1996). Voila, two mechanisms for OVs amongst others.

Although, viruses can't get all the credit for their therapeutic properties. Not only can viruses kill tumors, but the release of antigenic molecules from within lysed tumor cells cause the immune system to mediate further cancer cell destruction (Filley & Dey, 2017). The perfect recipe to help the immune system recognize tumors, provided by a successful OV.

Excellent, but has there been proof of concept? Designing new viral strains to administer patients may seem like a risk to their safety since it's not always known how the body can respond to a virus; however, by removing specific pathogenic genes in the virus adverse symptoms can be minimized. Fortunately, when adverse events do present, they resemble symptoms of the average flu with fatigue, chills, fever, and nausea, all of which were very manageable in clinical trials (Matsuda et al., 2018).

What has happened is that hundreds, if not more, patients with cancer have been treated on prospectively designed clinical trials using second and third generation OVs (Ta-Chiang et al., 2007). This is to say, we are quickly learning how to speak the language of virus and cancer on the level of DNA. With each generation of developed OVs we come closer to extending the lifespan of cancer victims. Soon enough, us, the clumsy bipedal humans, will have figured out a way to turn that pestering flu into what we may one day call, a cure for cancer.

Words: 605

Citations

Candelaria Gomez-Manzano, Juan Fueyo, Athanassios P. Kyritsis, Peter A. Steck, Jack A.Roth, Timothy J. McDonnell, Kim D. Steck, Victor A. Levin and W. K. Alfred Yung. (1996). Adenovirus-mediated Transfer of the *p53* Gene Produces Rapid and Generalized Death of Human Glioma Cells via Apoptosis. *Cancer Res*, (56) (4), 694-699.

Filley, A. C., & Dey, M. (2017). Immune System, Friend or Foe of Oncolytic Virotherapy?. *Frontiers in oncology*, *7*, 106. doi:10.3389/fonc.2017.00106

Matsuda, T., Karube, H., & Aruga, A. (2018). A Comparative Safety Profile Assessment of Oncolytic Virus Therapy Based on Clinical Trials. *Therapeutic Innovation & Regulatory Science*, *52*(4), 430-437.

Sarinella F, Calistri A, Sette P, Palu G, Parolin C. (2006). Oncolysis of pancreatic tumour cells by a gamma34.5-deleted HSV-1 does not rely upon Ras-activation, but on the PI 3-kinase pathway. *Gene Ther*. 13:1080–7.

Singh, P. K., Doley, J., Kumar, G. R., Sahoo, A. P., & Tiwari, A. K. (2012). Oncolytic viruses & their specific targeting to tumour cells. *The Indian journal of medical research*, *136*(4), 571-84.

Ta-Chiang Liu, Evanthia Galanis & David Kirn. (2007). Clinical trial results with oncolytic virotherapy: a century of promise, a decade of progress. *Nature Clinical Practice Oncology*, volume 4, pages 101–117.