VIROTHERAPY: Using virus for the cancer treatment

Nowadays, cancer is a matter of concern due to its large prevalence worldwide. According to WHO (World Health Organization), there are 14 million of new cases each year and this alarming amount is expected to increase. The high mortality rate is an evidence of the limitations of the current therapies, such as chemotherapy, radiotherapy or surgery. Therefore, novel therapies are needed and virotherapy is a promising one. This idea began to take hold in the 1950s, when the first trials with oncolytic viruses (OVs) where done. The results were encouraging, however, the interest diminished. At the present, the attention and trials of virotherapy are increasing.

1. MECHANISMS OF ACTION

TARGETING OV TO CANCER CELLS

- Specific cell surface receptor
- Antiviral immunity
- Phenotypic complementation
- MicroRNAs
- Tumor-associates proteins

SURVIVAL INTO CANCER CELL

- Normal cell
- Antiviral transcripts
- Cell cycle regulated
- Favourable environment for viral infection

CELL-DEATH MECHANISMS

- Direct
  - Apoptosis
  - Necrosis
  - Viral overload
- Indirect
  - Destruction of tumor vessels
  - Amplification of specific anticancer immune responses
  - Armed OVs

2. TYPES OF OVS

- Rational design
  - Using the “Hallmarks of cancer” and targeting tumor cells by phenotypic complementation or tumor-specific promoters.

- Bioselection
  - Libraries of novel OVs
  - Select plasmid OVs capable of entering cancer cell efficiently
  - Enrich the viruses
  - Screen the OVs to normalize
  - Select the candidates for development

- Obtaining OVs

- Rigtov®

3. DELIVERING OVS TO THE TUMOR

- Administration route
  - Intratumoral injection
  - Intravenous injection

- OVs have to surmount several barriers to exceed the virome threshold and become effective.

4. PHARMACOLOGIC TRIALS

5. COMBINED THERAPY

- OV administered with other therapies can produce synergic effects and enhance the efficacy. OVs can be used to sensitize cancer cells to other treatments or in resistant cells.

- CONCLUSIONS

  - Virotherapy provides a treatment whose specific target are the cancer cells. Although some viruses have innate tropism against tumor cells, this can be obtained by engineering.
  - Cancer cells have inactivated antiviral responses, therefore OVs are able to survive in them.
  - The lysis of the cells is achieved by direct cytolysis or stimulating the immunity system.
  - Although being quite safe, more clinical trials are required to properly determine its effectiveness.
  - The most promising OVs delivery is the intravenous, in this way a local treatment could be applied to a spread disease. This fact implies that the patient who has already been in contact with the virus, then develops NAS against it.
  - The therapy must be customized, studying each patient case individually. Moreover, there is the possibility of being used combined with other therapies acting in synergy.

Hence, virotherapy is considered a promising future treatment. Although further research on tumoral biology is required to find new targets where OVs could be directed, or investigate other virus strains that could act as oncolytic agents.

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