Generation and Validation of Anti-CD19 Single Chain Variable Fragment-Hydrophobin SpyTag-SpyCatcher Protein System for Targeted Drug Delivery to B-Cell Acute Lymphoblastic Leukemia

(Technical Report)

Co-production of Politics and Human-Derived Biological Material Donation and Use

(STS Research Paper)

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SocioTechnical Synthesis

B-Cell Acute Lymphoblastic Leukemia (B-ALL) causes around one thousand deaths per year, and only thirty to forty percent of patients achieve long term remission due to the lack of inexpensive and effective targeted treatments. To address this issue, our research team is designing a protein system that will solubilize and target anti-cancer drugs to the B-ALL cancer cells. This protein system is the combination of a hydrophobin protein (HFBI) and the short chain variable fragment (scFv) of the anti-CD19 antibody (FMC63scFv) that is linked through the SpyTag-SpyCatcher mechanism. HFBI is amphiphilic, so it can self-assemble around the hydrophobic anti-cancer drugs to solubilize them for drug delivery. FMC63scFv targets CD19 present on the B-cell lymphoblasts to deliver the anti-cancer drugs to the cells. This system would replace the need for a chemical surfactant that causes an immune reaction in the body. Additionally, it offers a more targeted therapy than the common treatment method of chemotherapy while being significantly less expensive than the targeted treatment of chimeric antigen receptor T cell therapy against CD19. With further validation, this protein system could offer a viable targeted drug delivery mechanism for B-ALL, as well as other CD19 positive cancers like chronic lymphoma leukemia and B cell non-Hodgkin's lymphoma.

Unlike some types of cancer, B-ALL offers the advantage of having a known biomarker, CD19, to help target the anti-cancer drugs to the cancerous area. For the other cancers, scientists are working to find a biomarker to improve treatment options. Having a biomarker allows the scientists to avoid systemic treatments that can also harm healthy cells. One way to find a biomarker is by sequencing tumor specimens to identify overexpressed or mutated genes specific to the cancer type. Scientists rely on donated tumor samples from patients to identify these biomarkers. They also rely on donated biological materials for tissue engineering research

applications and creating stem cells for a variety of medical and research purposes. Many policies have been created by academic, private, and governmental agencies to uphold patients' rights and to ensure that donated biological material specimens are of the highest quality so accurate data can be obtained. These policies, in conjunction with developments in medicine, should be designed with the goal of enhancing the welfare of the public, who are possible future patients. Through a historical analysis, I examined the co-production of science and politics surrounding the donation and use of human-derived biological materials in the United States from 1980 to 2020. I analyzed two cases that focused on patient rights, such as informed consent and ownership, and human embryonic stem cells, one of the most controversial examples of human-derived biological materials. Both cases highlight that there often is a gap between what is known and what is being done. Politicians may be trying to draft beneficial laws, but they also may lack the technical understanding to actually make the desired impact. The World Health Organization identified factors that help or hinder bridging this gap, therefore causing cooperation or conflicts respectively. Scientists and politicians can work to narrow this gap by working together and sharing information. However, there has to be a demand to communicate and share evidence from both sides. This communication is critical as science and politics are a complex, interwoven socio-technical system that have influenced one another over time. The two cases analyzed in this research paper show that the influence of science and politics on one another can either benefit or harm current and future patients. Therefore, proper communication between scientists and policymakers is critical to benefit patients by allowing progress in research to be made and creating more useful laws to protect patients.