

Synthetic Biology for Tumor Therapy

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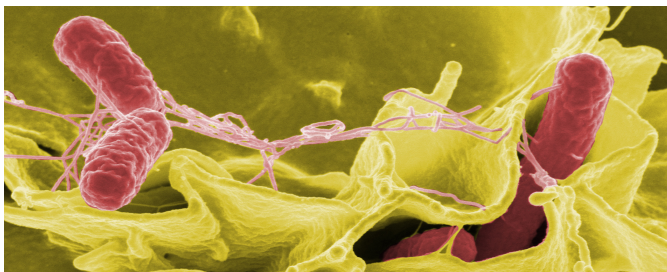
Abstract—Synthetic biology utilizes simple organisms whose genetic make-up can be manipulated to over-express certain gene products that would be beneficial to human health. These engineered cells can deliver anti-cancer drugs and enzymes to tumors directly while continuing to grow and develop as a bacterial population.

I. INTRODUCTION

In 2012 alone, over 1.6 million new cases of cancer were diagnosed in the United States. In the same year, over 500,000 people in the United States died of some form of cancer. The two most common treatments of cancer is chemotherapy and radiation, but both of these treatments have difficulty in fully reaching cancerous regions and distinguishing between healthy and harmful cells. Tumors will generally contain acidic and hypoxic regions, meaning that oxygen is not able to reach all parts of the cancerous tissue; conditions that make the delivery of anti-cancer agents very difficult. Strangely, it was discovered that populations of Salmonella grow in these anaerobic regions a thousand times faster than in any other part of the body. Synthetic biology involves taking these simple Salmonella typhimurium organisms and redesigning their cellular circuits and gene expressions in order to release chemicals that will destroy cancerous tumors.

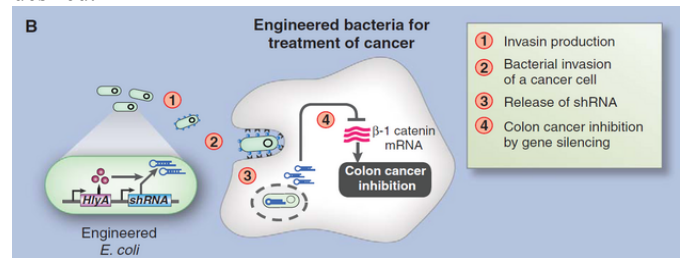
II. METHODS

Mutated strains of *S. typhimurium*, which have been found to not be harmful to human cells and could be slowly and completely eliminated from the host normal tissue, contains a cellular pathway that controls the injection of proteins into human cells. Through rewiring of genetic circuits that code for these proteins, engineers can create a genetic pathway that codes for cytotoxic, anti-cancer proteins that will release these drugs only when attached to a promoter molecule specifically present in tumor cells only. These cells must also be changed to suppress an immune system response, so that the bacteria cells are not destroyed before attacking the tumor. Genetically, *S. typhimurium* is very similar to *E. coli*, making it relatively easy to modify and engineer to release the desired cytotoxic drugs. Before human use, these same strains of bacteria are tested in mice using a green colored, easily traceable protein product in order to make certain that they do not grow on healthy cells and release cytotoxins only when in or on tumors.



III. RESULTS

Genetically engineered Salmonella has not yet been used for human tumor therapy, but the process itself, which has been tested in mice, is very promising. The bacteria will release cytotoxic drugs into cancerous cells in an effective way, and in a faster way than previously used *E. coli* cells, which were modified for tumor therapy in earlier trials. While the genetic makeup and cellular processes are well mapped in Salmonella, it is still quite difficult to isolate biological systems, like electrical circuits are in machines. Often times, directed evolution must be used as a trial-and-error process to make sure that even though some biological circuits will interfere with others, the overall product will be the one that is desired.



IV. DISCUSSION

Genetic engineering in bacterial cells for tumor therapy is relatively new; scientists were just starting to test its effectiveness on tumors in mice in 2007. In the past, manufacturing the biological parts needed to modify each bacterium had to be tested and built from scratch, which was a long and slow process, making this method of cancer treatment very cost and time ineffective. Within the past few months, though, scientists from Imperial College in England have found a way to mass-produce genetic parts of simple organisms, instead of having to re-engineer a cell every time a new part needs to be made. These mass produced parts can be simultaneously tested in cell-like environments within test tubes. At the same time, over 100 organizations are calling for the process of Synthetic Biology to be suspended overall, saying that serious government regulations of the safety of the workers, environment, and the nature of the synthetic organisms needed to be put in place, and until then, synthetic biology needs to be suspended.

REFERENCES

- [1] "Discovery in Synthetic Biology Takes Us a Step Closer to New 'Industrial Revolution'" *ScienceDaily*. ScienceDaily, 31 Jan. 2013. Web. 28 Mar. 2013.
- [2] Nabil, Arrach. "Engineering Salmonella for Lung Cancer Therapy." *TRDRP Grant*. Sidney Kimmel Cancer Center, 2007. Web. 28 Mar. 2013.
- [3] Pennisi, Elizabeth. "111 Organizations Call for Synthetic Biology Moratorium." *ScienceInsider*. N.p., 13 Mar. 2012. Web. 28 Mar. 2013.
- [4] Prindle, Arthur, Jangir Selimkhanov, Tal Danino, Phillip Samayoa, Anna Goldberg, SangeetaN. Bhatia, and Jeff Hasty. "Genetic Circuits in Salmonella Typhimurium." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 09 Aug. 2012. Web. 28 Mar. 2013.
- [5] Trafton, Anne. "MIT Team Builds Most Complex Synthetic Biology Circuit Yet." *MIT's News*. MIT News Office, 7 Oct. 2012. Web. 28 Mar. 2013.

