INTRODUCTION

Cancer is the leading cause of death worldwide and one of the most challenging aspects of cancer medicine is the difficulty of drug delivery. The cancer medicine of today is not specific for cancer cells, but kills healthy cells as well. We therefore wanted to develop a system for specific drug delivery, to show that one of the most challenging medical problems can be solved by designing a genetic circuit which enables an E. coli cell to detect and attack cancer cells. The basic idea is that the cell will produce a cancer toxin constitutively and the toxin should only be released if cancer cells are present, and never otherwise. To make this happen, the E. coli cells will undergo lysis when they detect a cancer specific environment.

To destroy cancer cells, we needed a toxin, and for this purpose, colicin was chosen. Colicins are toxins produced by some strains of E. coli to suppress the growth of competing strains. For our project, we needed an isolated colicin part, so we made the part BBa_K822002 [3][4]. This biobrick contains the colicin code, in addition to a colicin immunity protein. Our colicin brick was designed to be used in a genetic circuit where it is induced by a cancer specific environment.

The detection of cancer cells is based on finding regions having high lactate concentration and low oxygen concentration [1]. These two cues were chosen to initiate transcription of two different proteins. Together, the proteins should activate the unit responsible for lysis. If only one of the cues are present, the cells will not lyse. This keeps the toxin from being released in high amounts when no cancer cells are present.

Search

- O2: For the purpose of recognizing surroundings with low oxygen concentration, a microaerobic vgb promoter from Vitreoscilla sp. was used. This promoter has its highest effect at oxygen levels of about 5% [5].
- Lactate: To recognize surroundings having high concentrations of lactate, we decided to make two new promoters; one of them being the lld promoter from E.coli, and the other being the ldhA promoter from C.glutamicum. Both promoters were sent to a model of the full system (figure 2.) The results show that the system can detect cancer specific environments.

Our goal for iGEM 2012 has been to create a genetic circuit which enables an E. coli cell to detect and attack cancer cells. The basic idea is that the cell will produce a cancer toxin constitutively and the toxin should only be released if cancer cells are present, and never otherwise. To make this happen, the E. coli cells will undergo lysis when they detect a cancer specific environment.

SEARCH AND DESTROY

Our goal for iGEM 2012 has been to create a genetic circuit which enables an E. coli cell to detect and attack cancer cells. The basic idea is that the cell will produce a cancer toxin constitutively and the toxin should only be released if cancer cells are present, and never otherwise. To make this happen, the E. coli cells will undergo lysis when they detect a cancer specific environment.

To destroy cancer cells, we needed a toxin, and for this purpose, colicin was chosen. Colicins are toxins produced by some strains of E. coli to suppress the growth of competing strains. For our project, we needed an isolated colicin part, so we made the part BBa_K822002 [3][4]. This biobrick contains the colicin code, in addition to a colicin immunity protein. Our colicin brick was designed to be used in a genetic circuit where it is induced by a cancer specific environment.

The detection of cancer cells is based on finding regions having high lactate concentration and low oxygen concentration [1]. These two cues were chosen to initiate transcription of two different proteins. Together, the proteins should activate the unit responsible for lysis. If only one of the cues are present, the cells will not lyse. This keeps the toxin from being released in high amounts when no cancer cells are present.

Search

- O2: For the purpose of recognizing surroundings with low oxygen concentration, a microaerobic vgb promoter from Vitreoscilla sp. was used. This promoter has its highest effect at oxygen levels of about 5% [5].
- Lactate: To recognize surroundings having high concentrations of lactate, we decided to make two new promoters; one of them being the lld promoter from E.coli, and the other being the ldhA promoter from C.glutamicum. Both promoters were sent to a model of the full system (figure 2.) The results show that the system can detect cancer specific environments.

The full system was divided into three parts; lld promoter, vgb promoter and holin production. The three parts were then combined to a model of the full system (figure 2.) The results show that the system can detect cancer specific environments.

MOELLING

The full system was divided into three parts; lld promoter, vgb promoter and holin production. The three parts were then combined to a model of the full system (figure 2.) The results show that the system can detect cancer specific environments.

OUTREACH

For the outreach part of our project, we participated in "Researchers' Night". This is an event for high school students, to get an introduction into the world of science.

LITERATURE

[6] BioBrick part BBa_K112808, designed by the UC Berkeley iGEM 2008