ידע חברה למחקר ופיתוח בע"מ
מסחור טכנולוגיות של מכון ויצמן למדע
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TECHNOLOGY TRANSFER FROM THE WEIZMANN INSTITUTE OF SCIENCE

## An approach to express genes via a phage communication system:

# A Novel Method for Controlling Gene Expression

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| **Project Number:** | 1847 |
| **Principal Investigator:** | Prof. Rotem Sorek |
| **Patent Status:** | Pending |
| **Last Updated:** | 2018-01-29 (3) |

## Overview

A method for controlling gene expression using a novel phage-based transcription factor-peptide system.

A fundamental challenge of synthetic biology and its clinical applications, is the capability to control gene expression. Presently, gene expression systems for research and industry have several limitations, such as a small number of available systems, inconsistent behavior among systems, and the requirement for high concentrations of a signaling molecule to induce/repress a gene. **Consequently, there is a strong need for a better and diverse array of gene expression systems.**

The team of Prof. Sorek at the Weizmann Institute of Science (WIS) has made the paradigm-shifting discovery that phages (viruses) have a quorum sensing system, similar to that found in bacteria. The novel system, named *Arbitrium* by the Sorek team, communicates to said phages, indicating whether a lytic or lysogenic cycle is to be entered. The *Arbitrium* system has a wide range of synthetic-biology and biotechnological applications.

## The Unmet Need

Presently, there is a constrained number of methods for controlling synthetic gene expression, including lac, ara, and others. However, many of these expression systems have flaws in terms of efficiency and specificity. Additionally, said gene expression systems lack consistency in terms of behavior relating to leakage and dynamic range of expression, which, subsequently hampers their application in externally controllable synthetic gene networks.

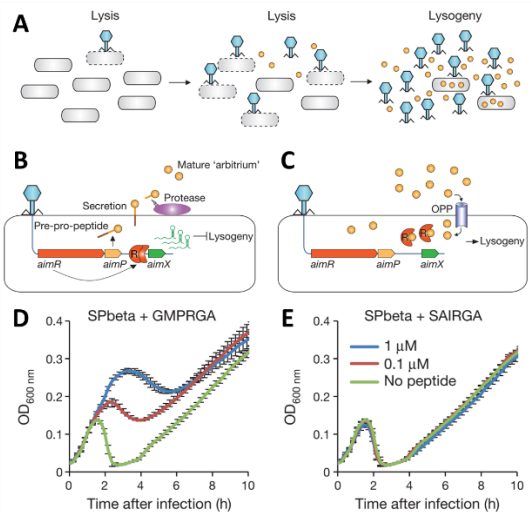
## The Solution

Prof. Sorek's research team has discovered the unique *Arbitrium* system, a phage quorum sensing system that enables specific control of gene expression.

### Technology Essence:

Temperate phages can infect bacteria either in a lytic cycle, which lyses the bacterial wall, or in a lysogenic cycle in which the phage genome integrates into the bacterial genome. The research team of Prof. Sorek discovered the novel *Arbitrium* communication system that enables lytic or lysogenic cycle (Fig. A). The *Arbitrium* system functions on the basis of three genes, *aimR*, *aimP*, and *aimX*. AimR is a dimeric receptor that binds and activates the transcription of gene *aimX*, whereby AimX inhibits lysogeny leading to lysis (Fig. B). AimP is a pro-peptide (arbitrium peptide) that is expressed following infection, secreted extracellularly, and post-translationally modified. After the arbitrium peptide accumulates to a specific concentration, it is internalized and bound by the AimR receptor, which inhibits the expression of AimX and leads to lysogeny (Fig. C). The Sorek team further determined that when infected bacteria are incubated with the arbitrium peptide from the same phage that infected them, the bacterial growth curve changes due to a shift to a lysogenic cycle (Fig. D). However, when

incubated with an arbitrium peptide from a different phage, the bacterial growth curve does not shift, regardless of peptide concentration (Fig. E).




**A) Schematic of arbitrium peptide accumulation during phage infection of bacteria. B) Post-infection *aimR* and *aimP* expression leading to lysis and AimP accumulation. C) At later stages after infection, lysogeny is preferred due to inhibition of AimX expression. D-E) Growth curves of *B. subtillis* in the presence of Phage SP Beta with either its corresponding arbitrium peptide (D) or arbitrium peptide from the phi3T phage (E). (Image modified from Erez Z, et al. Nature. 2017 Jan 26;541(7638):488-493. doi: 10.1038/nature21049. Epub 2017 Jan 18)**

## Applications and Advantages:

- **Unique system –** Effectively induces or shuts off expression of a gene.
- **Standard Chemistry –** Uses regular peptides, therefore standard synthesis can be used.
- **Wide Dynamic Range**
- **Over 100 Different Systems**
- **Uniformity Among Systems**

## Development Status

Prof. Sorek and his team identified and characterized the *Arbitrium* communication system. They have deciphered the transcription factor-peptide pair mechanism by which the *Arbitrium* system functions, and further identified over 100 different transcription factor/peptide pairs.

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