

# LICENSING OPPORTUNITY

ETH transfer – Linking Science and Business

## Towards increased patient compliance - A drug delivery implant with adjustable transdermal control by phloretin

### Keywords

Engineered cell implants, Subcutaneous implants, Topical delivery, Transdermal gene regulation, Phloretin, Transgene expression

### Background

So far, several heterologous transcription modalities have been developed which are responsive to injection based or oral inducers. Transdermal and topical delivery of inducer molecules have not been reported yet and will provide considerable advantages.

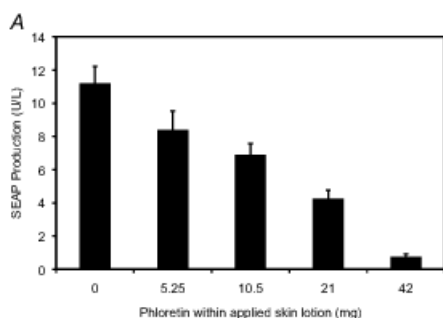


Fig. 2: PEACE-controlled transgene expression in mice was shown to be phloretin dependent. Phloretin was applied on the skin in different concentrations and has led to a negative regulation. The concentration of phloretin applied on the skin was resp. 0%, 3.1%, 6.25%, 12.5% and 25% (in Vol %).



Fig. 1: A subcutaneous gene network can be controlled and adjusted by applying a skin cream containing the inducer phloretin.

### Invention

This invention consists of an encapsulated cell implant containing a gene construct (Fig. 3) that can be induced by an external trigger. The inducer can be added in a very convenient way by topical delivery (Fig. 1) which leads to transdermal gene regulation. Constructs can be designed in order to have a positive or negative control (Fig. 3) mechanism upon applying an inducer.

Phloretin is a natural antioxidant found in apples in very low concentrations, this molecule makes cell walls more permeable and can easily diffuse through the skin of mice (Fig. 2) and human. A phloretin-adjustable control element (PEACE) (Fig. 2 and 3) has been designed, that reacts very fast on the transdermal inducer. The transdermal and topical delivery of the inducer molecule phloretin will provide several advantages such as convenience, improved patient compliance and elimination of hepatic first-pass effects.

### Patent Status

- Patent pending PCT

### Features & Benefits

- Adjustable and controllable subcutaneous gene networks with topical delivery of phloretin
- Improved patient compliance and convenience
- Circumventing disadvantages of oral administration of drugs
- Implants of a huge diversity can be designed positively or negatively controlled by phloretin
- Phloretin is a natural product

### Field of Applications

Short term:

- Multifunctional protein expression vector with phloretin as inducer in:
  1. Functional genomic research
  2. Drug discovery
  3. Protein expression and manufacturing

Long term:

- Gene therapy applications e.g. treatment of inflammatory diseases, cancer, metabolic diseases, etc.
- Design of complex synthetic gene networks

P.t.o. →

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## Towards increased patient compliance (cont.)

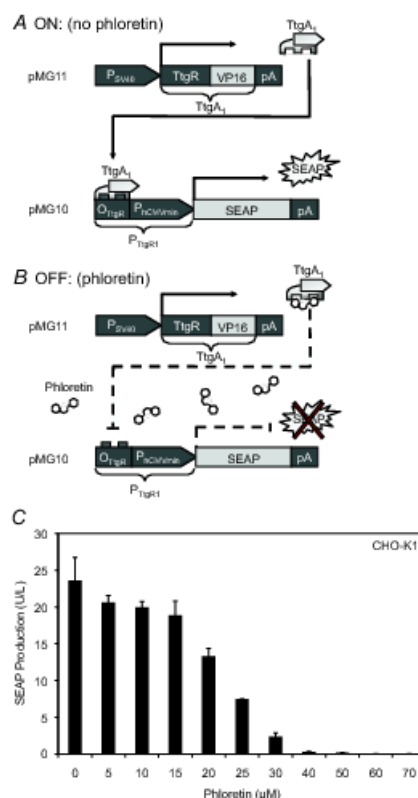


Fig. 3: The PEACE-construct consists of two genetic constructs, one for the constitutive expression of the synthetic mammalian PEACE transactivator and one reporter construct encoding the gene of interest under the control of the PEACE inducible promoter. A. Without the inducer phloretin SEAP is produced at a constant level, B. As soon as phloretin is present, the construct will stop the SEAP production, C. SEAP expression in mammalian cells containing the PEACE construct is directly dependent on the phloretin concentration present in the different cultures.

## References

- Gitzinger, M., Kemmer, C., El-Baba, M.D., Weber, W., Fussenegger, M. Controlling transgene expression in subcutaneous implants using a skin lotion containing the apple metabolite phloretin. PNAS, June 2009, Vol.106, no. 26, 10638–10634