Multi-Growth Factor Releasing Hydrogel System Controlled by DNA Hybridization
“Cells as building blocks”

“Polymer scaffolds as blueprints”
Limitations in the Field

- Lack of Suitable Methods to Delivery GF *in vivo* (Kasemkijwattana et al., 2000)

- Delivery Requirements:
  - 2 GF simultaneously
  - adjustable rates
  - prolonged release
  - minimal degradation

(Bourque et al., 1993; Bostrom et al., 1995; Yu et al., 2002; Chen et al., 2009)
Develop and test an affinity-based release system for releasing multiple Growth Factors (GF) *in vivo*.
Capitalizing on chemical interactions between the drug and the delivery system to control drug release rates.

(Wang and von Recum, 2011)
Affinity-Based Release System
Hydrogel

Advantages:
- Mechanical strength
- Degradability
- Biocompatibility
- Injectable formulation
  (Crompton et al., 2007; Costa et al., 2011)

Our 2-Pronged Attack
- GF loading device
- Tissue scaffold

Collagen hydrogel

DNA Hybridization

Factors:

- pH
- Salt concentration
- GC content
- Strand length
- Temperature

(Clausen-Schaumann et al., 2000; Chalikian et al., 1999)
The “Big” Picture

Key:
- HT DNA
- LT DNA
- GF₁
- GF₂

Hydrogel
Experimental Design

1) Confirmation of Chemistry in 2-D Model
2) Study of DNA Melting Temperatures
3) Growth Factor Release
Converting inorganic glass to useful thiol
1) Confirmation of Chemistry in 2-D Model

Adding hydrogel followed by one strand of DNA

Converting inorganic glass to useful thiol
1) Confirmation of Chemistry in 2-D Model

Introducing **growth factors** synthesized with the complementary DNA

Adding **hydrogel** followed by one strand of **DNA**

Converting inorganic glass to useful **thiol**
2) Study of DNA Melting Temperatures

- Tm: 50% duplex
- Gradual heating (30-80°C)
- Hypochromism
- DNA absorbance at 260nm

Table 1: Oligonucleotide Label Key

| High Melting Temperature Strands (HT) | HTA     | GGC TGT GCC CGG TCG |
| Low Melting Temperature Strands (LT) | LTA     | AAA GAT AAG TAA CAA |
|                                      | HTB     | CGA CCG GCC ACA GCC |
|                                      | LTB     | TIG TIA CTT ATC TTT |

*All strands contain a thiol group at the end of the sequence

http://www.ifa.hawaii.edu/UHNAIimages/boal-figures/figure22.jpg
2) Study of DNA Melting Temperatures

![Graph showing absorption at 260 nm vs. temperature for DNA samples with different GC content.](image)

DNA: LTA - LTB

$T_m = 44.43$

Low GC

DNA: HTA - HTB

$T_m = 65.98$

High GC
3) Growth Factor Release
Conclusions

- Successful in vitro release results!
  - Novel method of DNA-affinity release
  - Significant variations in release rates

- Making strides in the developing field of Tissue Engineering
What’s Next?

- Further *in vitro* testing
  - Other DNA sequences
  - Multiple fluorescently labeled GFs
  - Real GFs
- *In vivo* testing
  - Animals followed by humans


