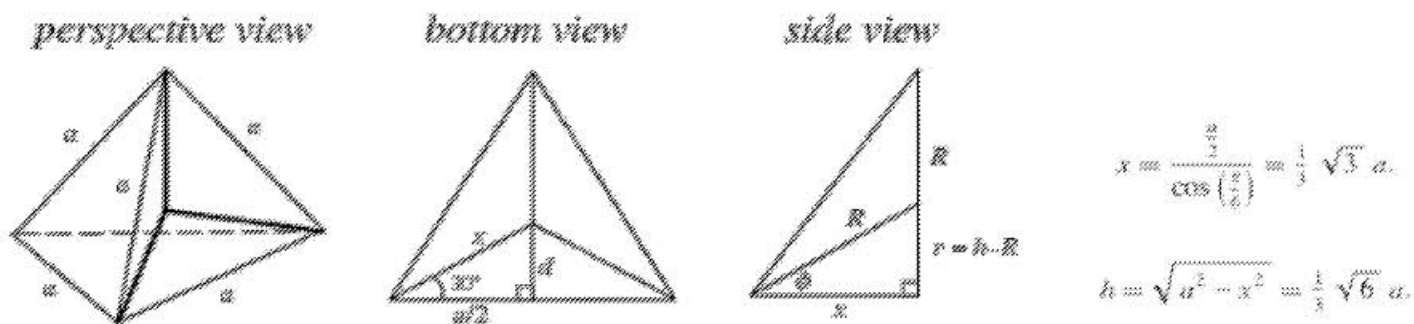


Tetrahedral Geometry



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Fig. 1

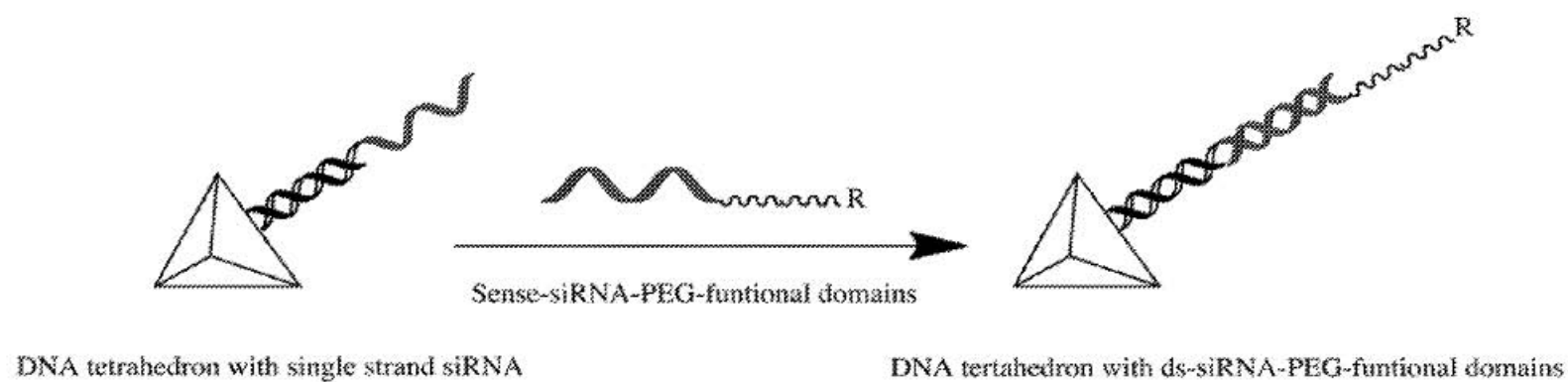


Fig. 10

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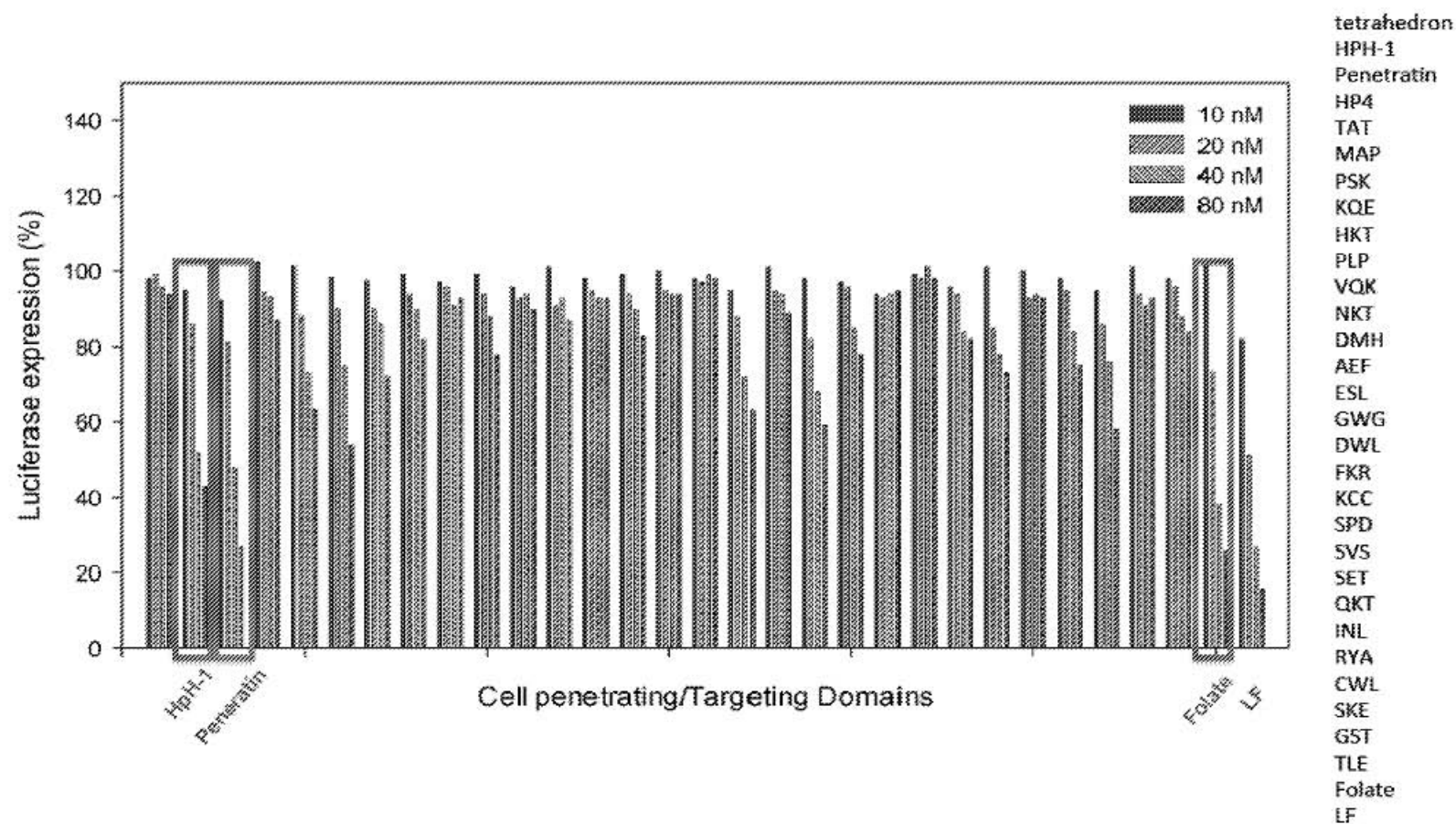
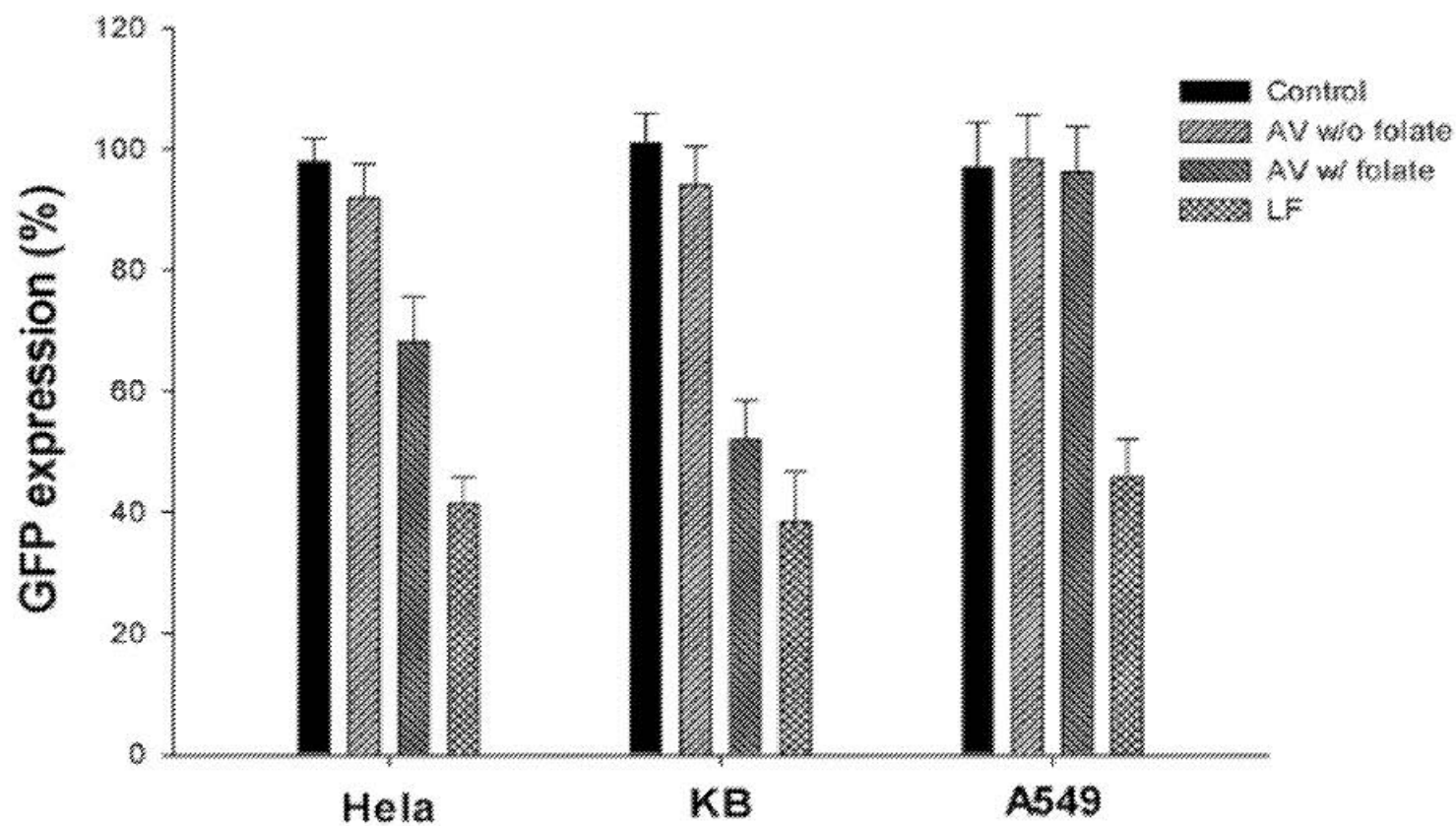
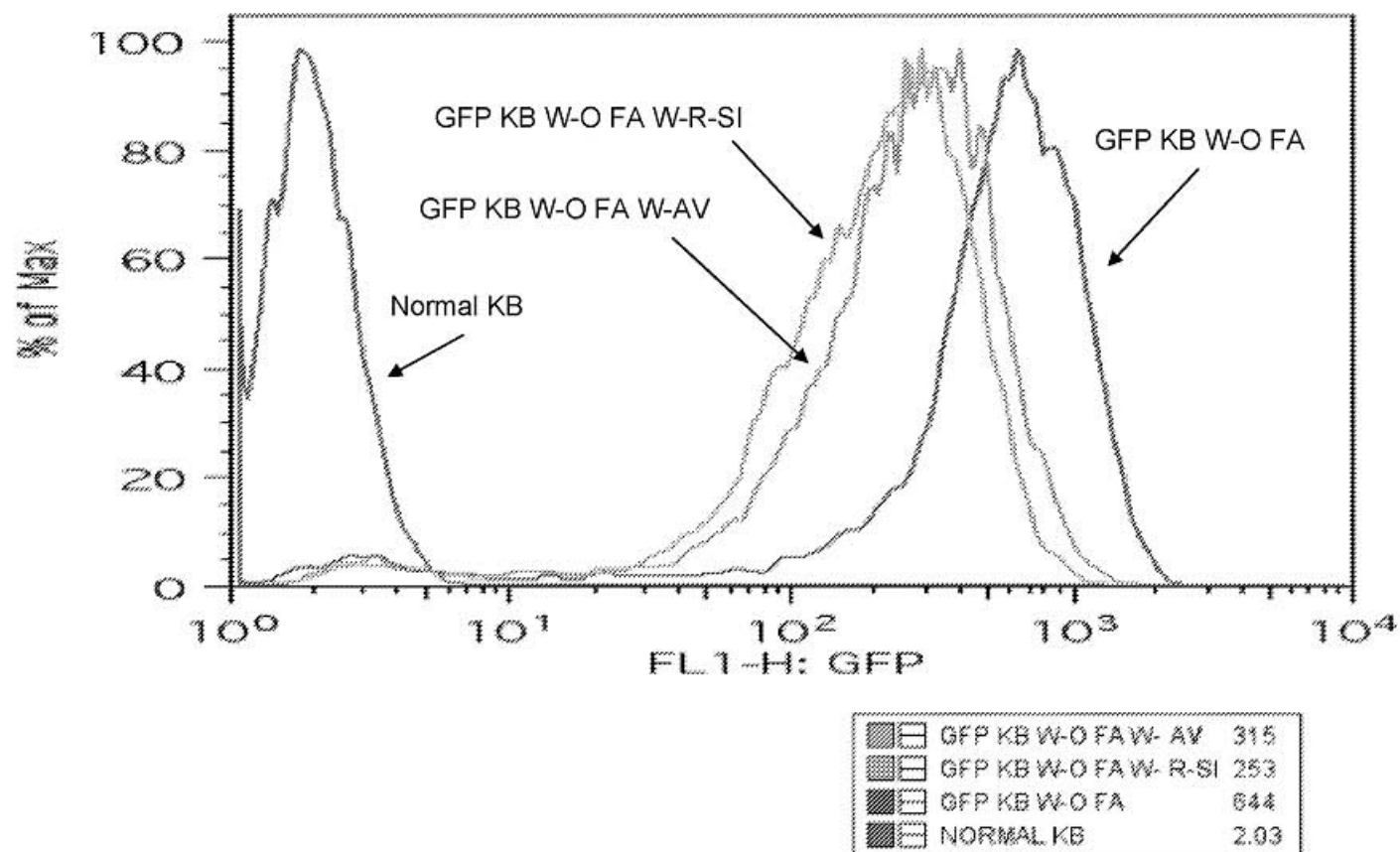


Fig. 11



with 50 nM anti-GFP-siRNA in folic acid free medium

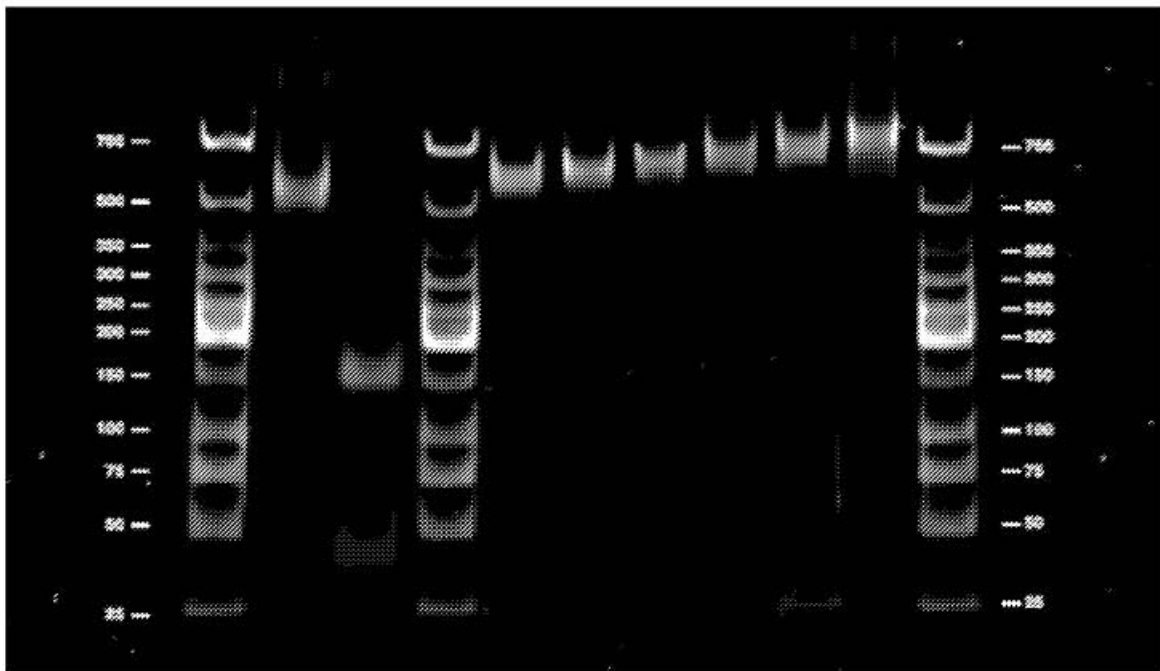
Fig. 12



with 50 nM anti-GFP-siRNA in folic acid free medium

Fig. 13

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Assembly of Folate Conjugated siRNA
Tetrahedron

Fig. 14

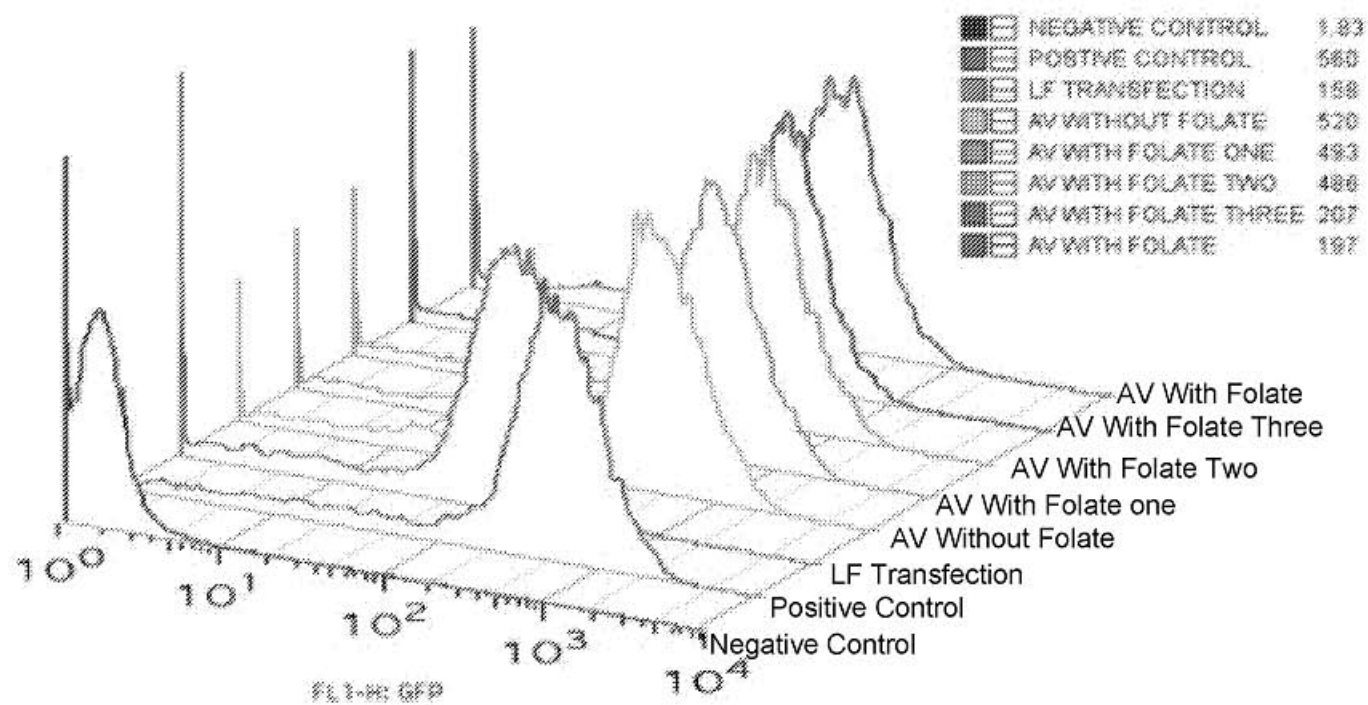


Fig. 15

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Higher Order Tetrahedral Structures

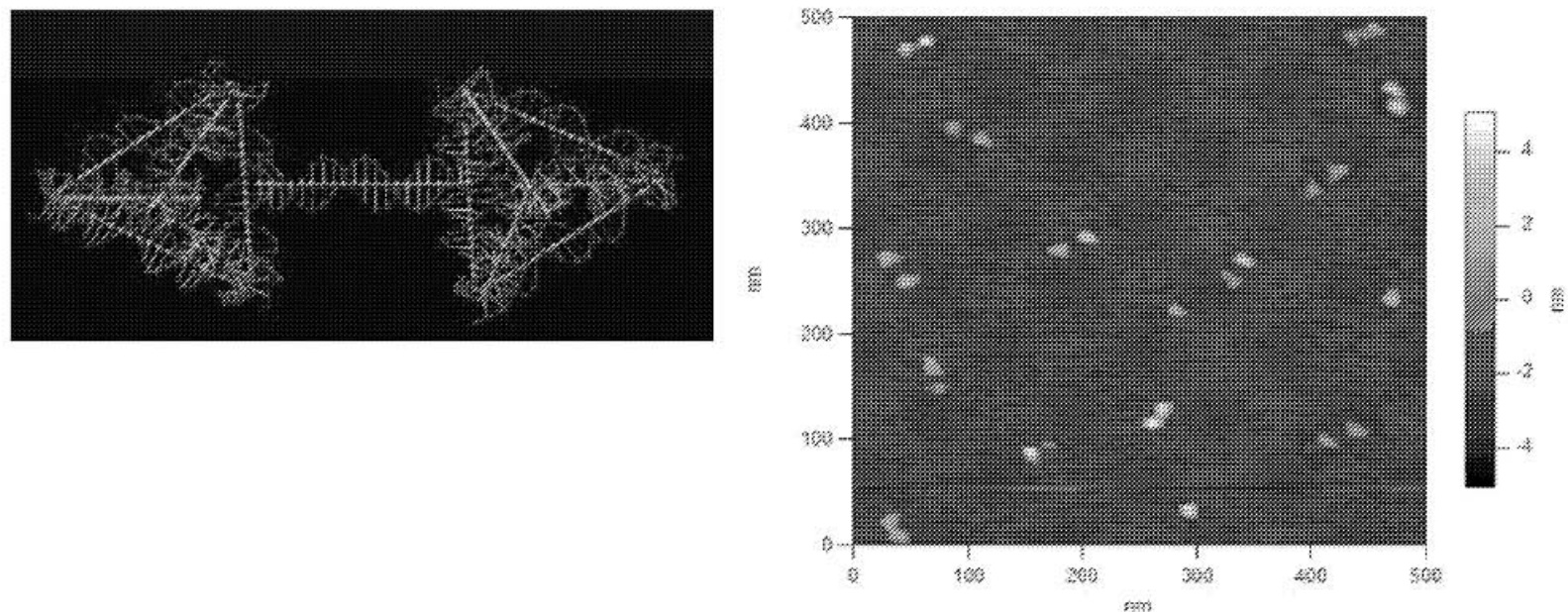


Fig. 16

Higher Order Tetrahedral Structures

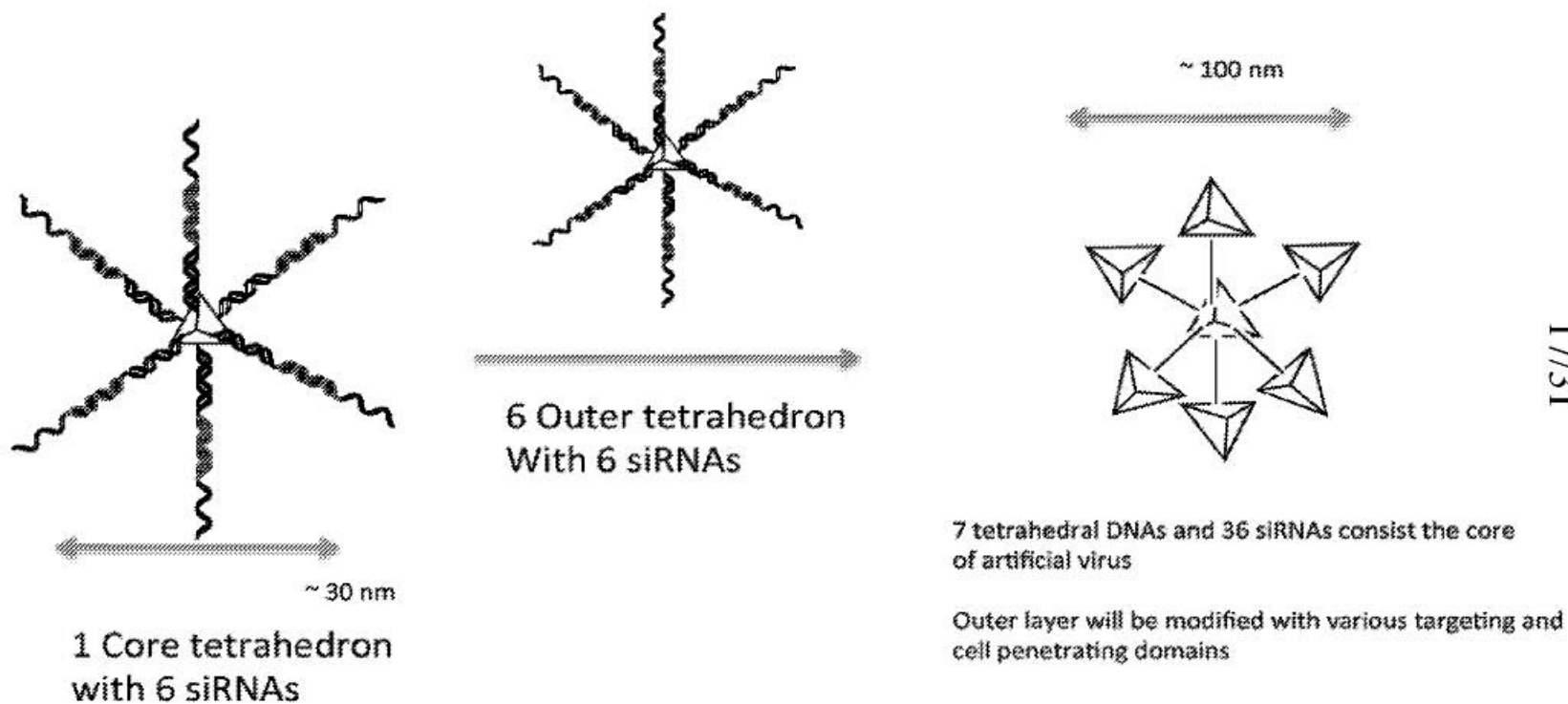


Fig. 17

Assembly of Higher Order Tetrahedral Structures

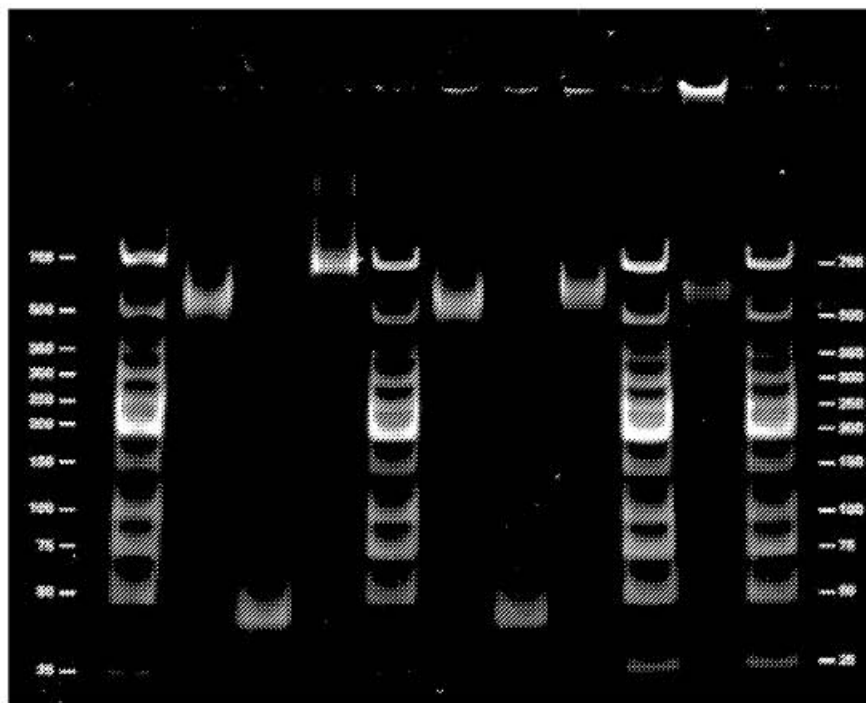
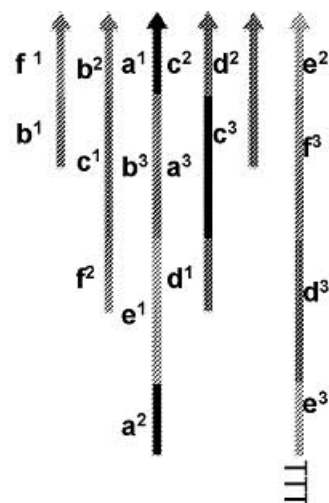
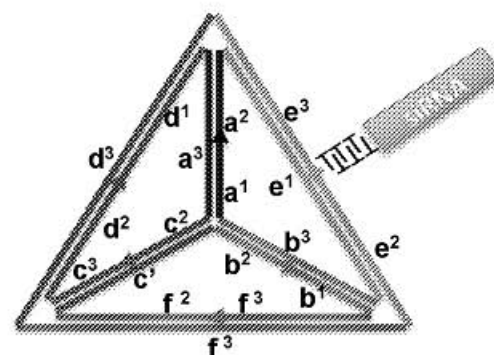


Fig. 18

single strand oligonucleotides



TTT 
 one-step self-assembly



Molecularly identical nucleic acid nanoparticle

Molecularly identical nucleic acid
nanoparticles

Fig. 19

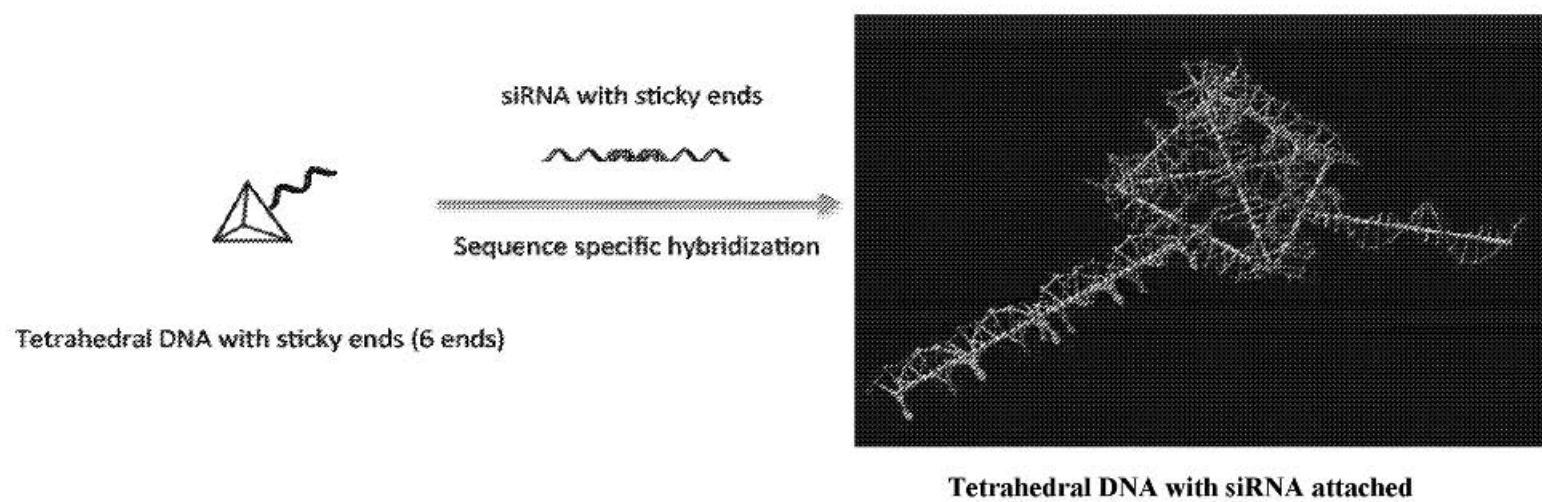


Fig. 2

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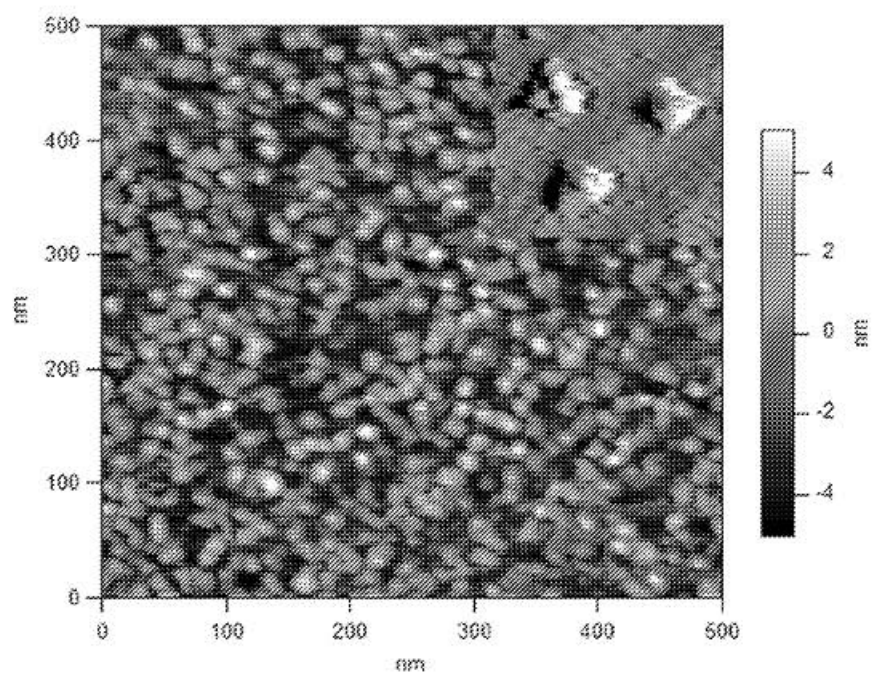


Fig. 20

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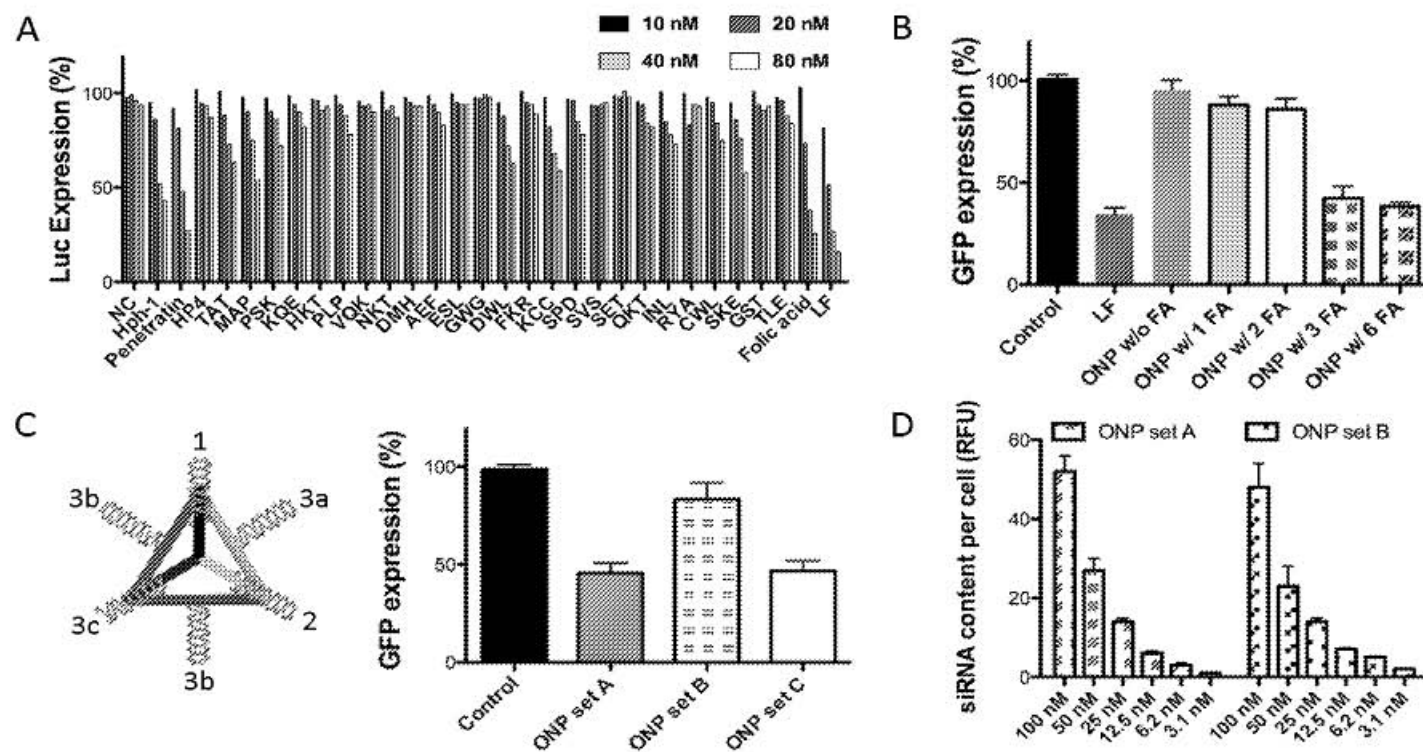
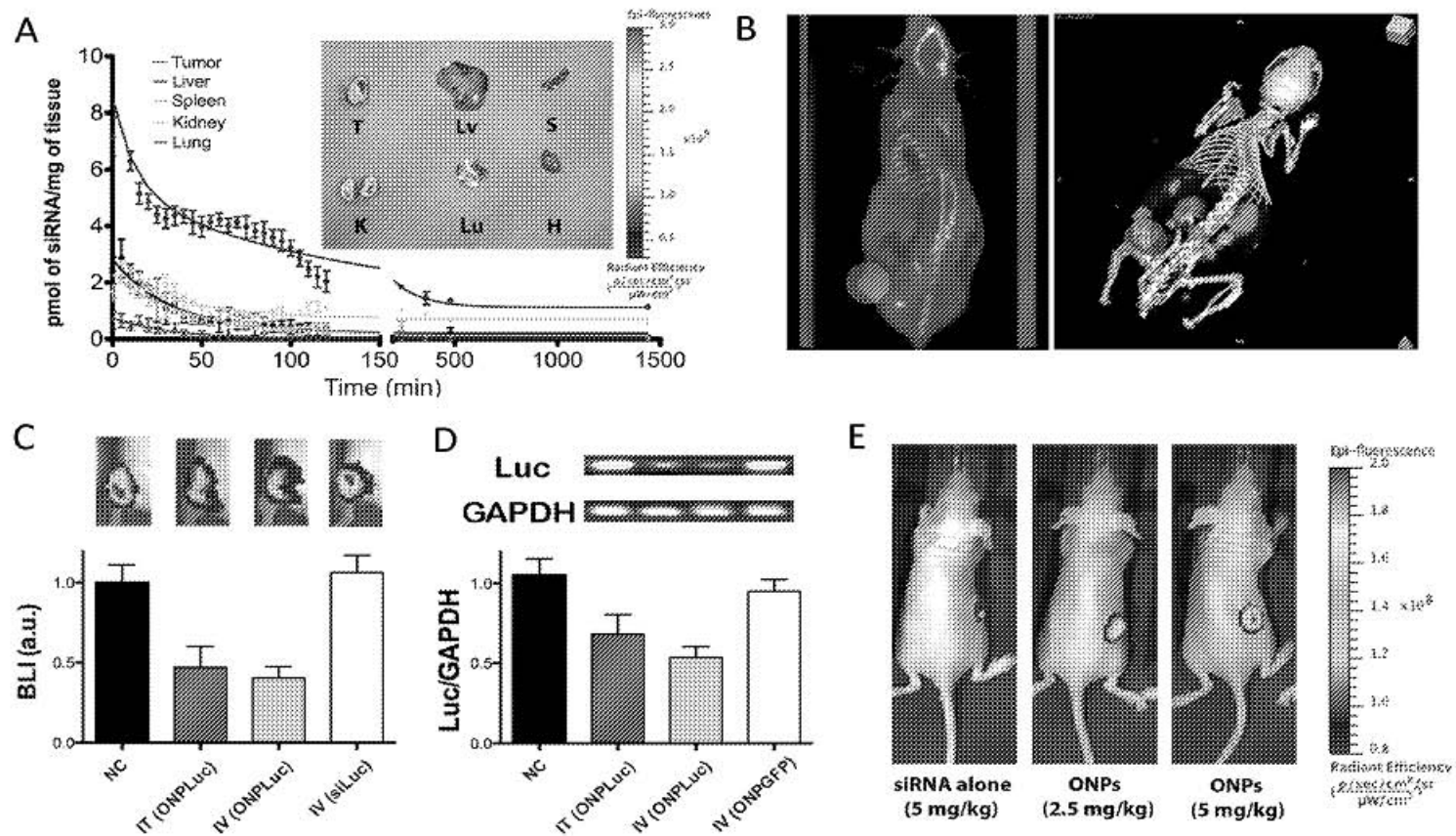


Fig. 21



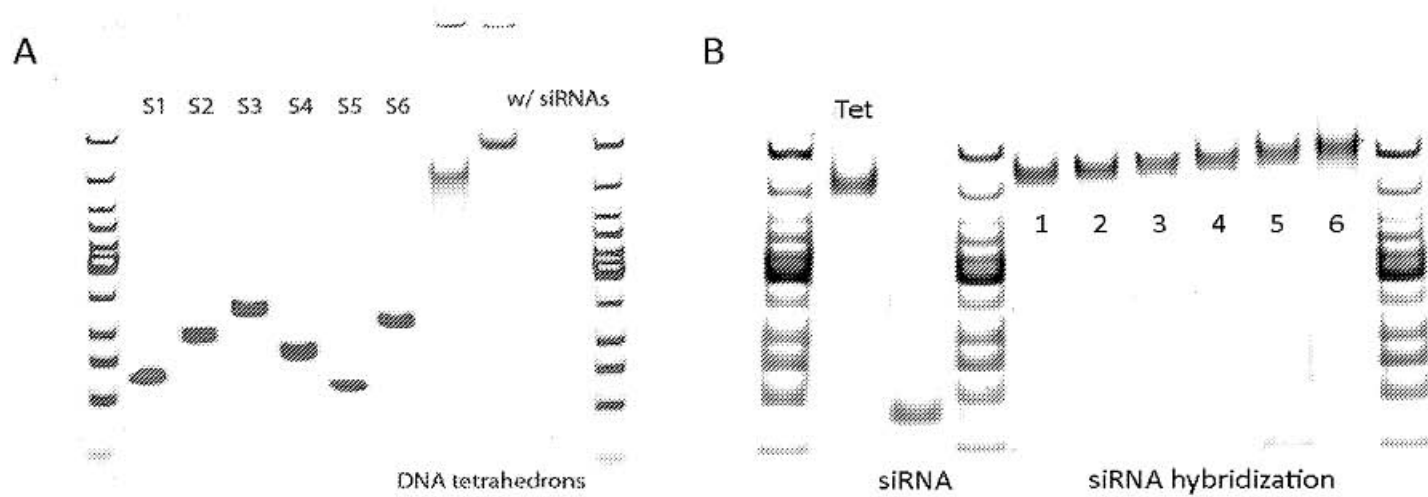


Fig. 23

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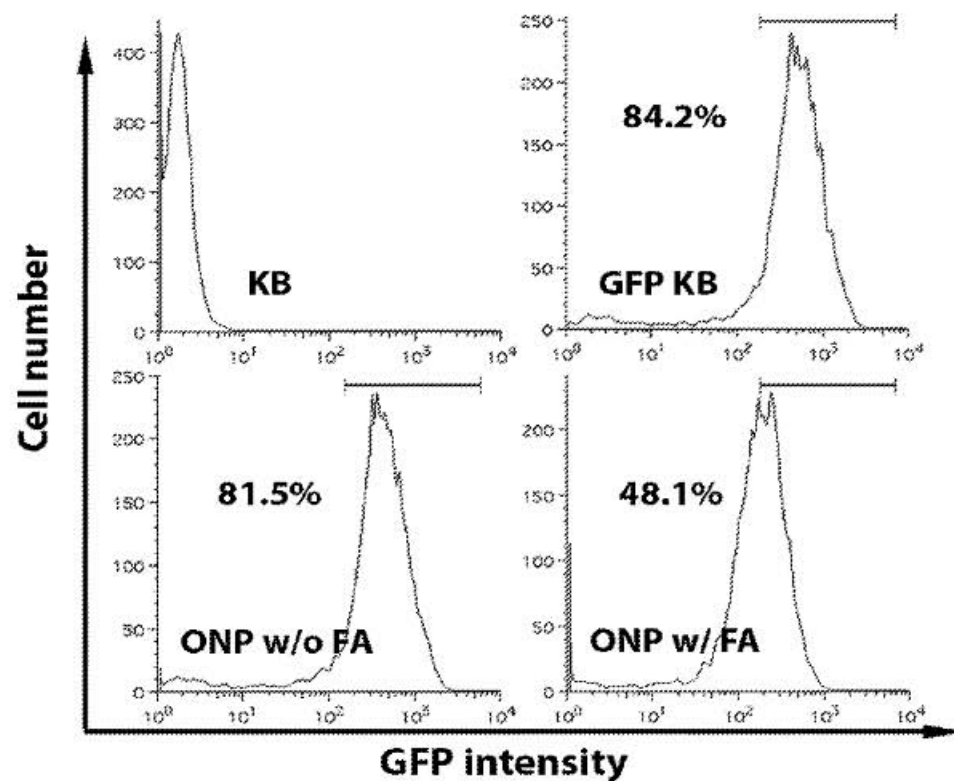


Fig. 24

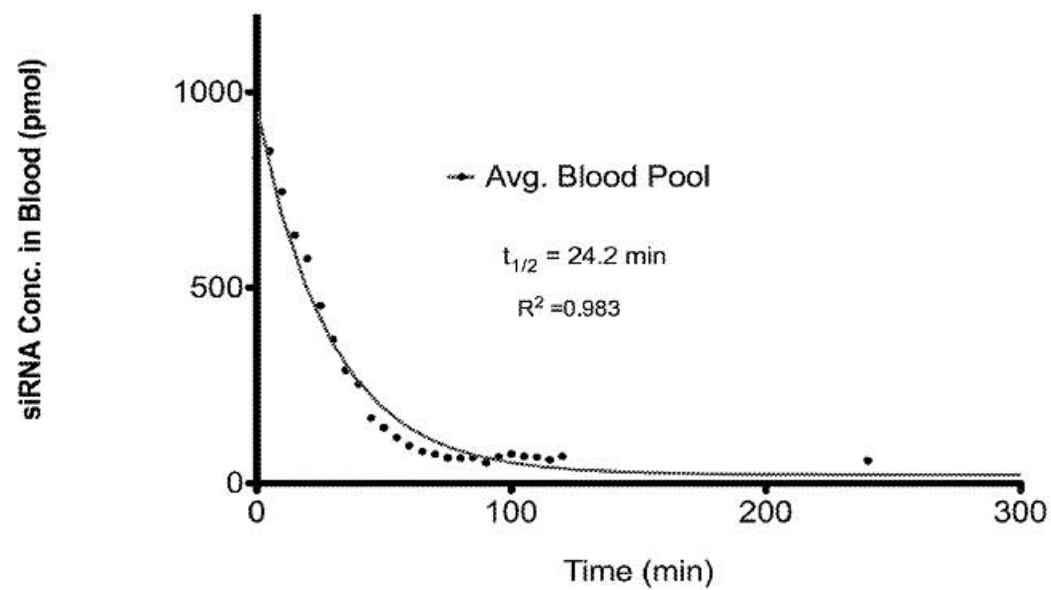


Fig. 25

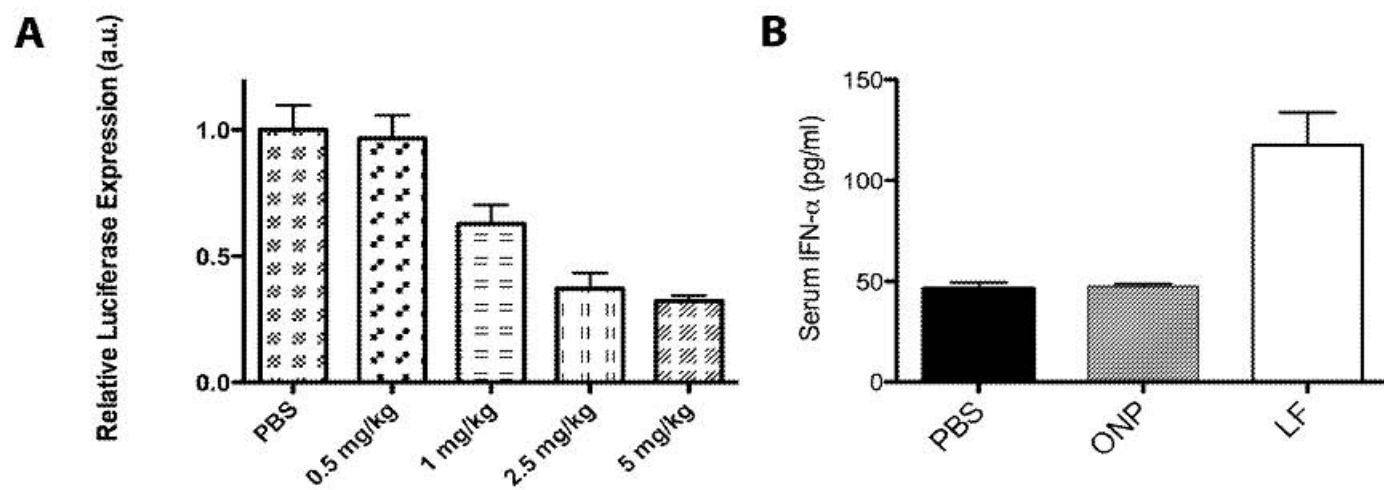


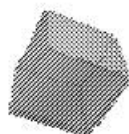
Fig. 26

Alternative Oligo-Nucleic Acid Nanoparticle (ONP) Shapes

Symmetrical Polyhedron shapes:



tetrahedron



Cube or
hexahedron



octahedron



dodecahedron



icosahedron

Stellation Polyhedron shapes:

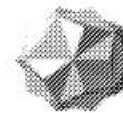
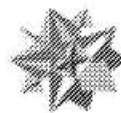
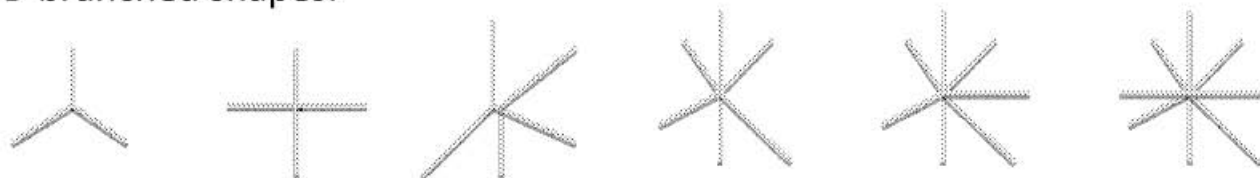


Fig. 27

Alternative Oligo-Nucleic Acid Nanoparticle (ONP) Shapes

3D branched shapes:



2D shapes:



N = 3

4

5

6

7



8



10



12



Circle

Fig. 28

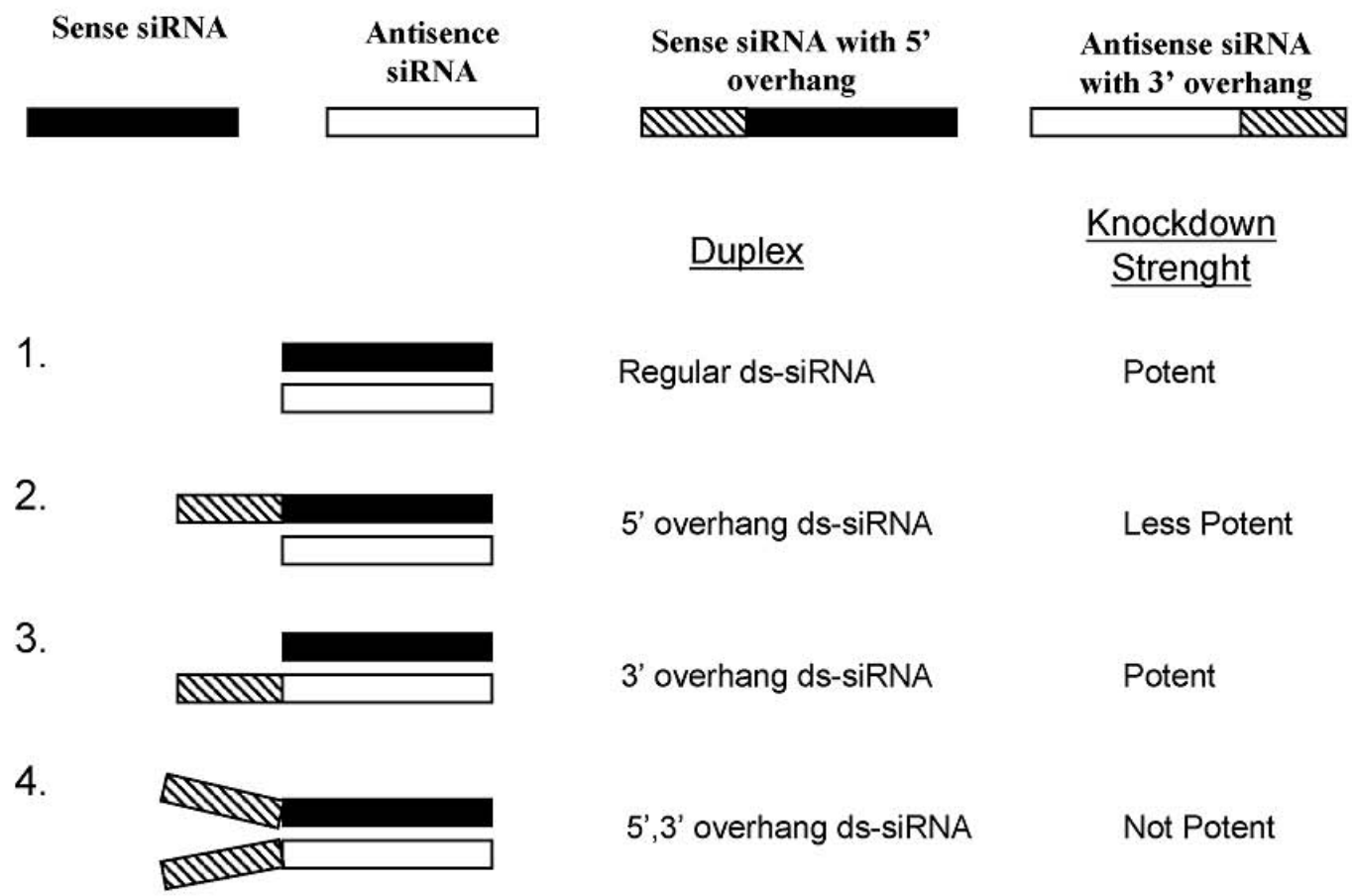
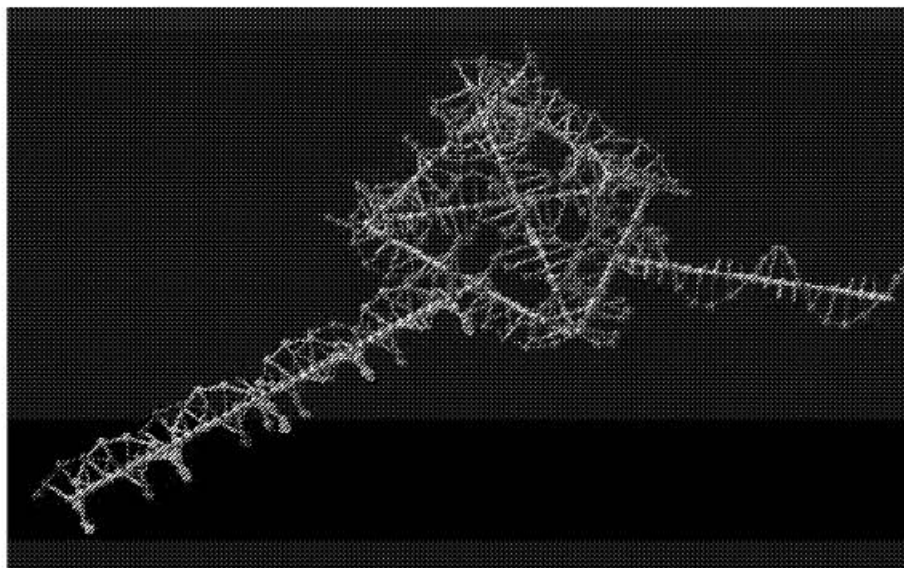


Fig. 29



- DNA hybridization allows precise control of polyhedron geometry
- Defined and relatively easy modification on spacing and spatial orientation of RNA, functional moiety, and others
- DNA/RNA nanoparticles can be used as a building block for higher order structure

Fig. 3

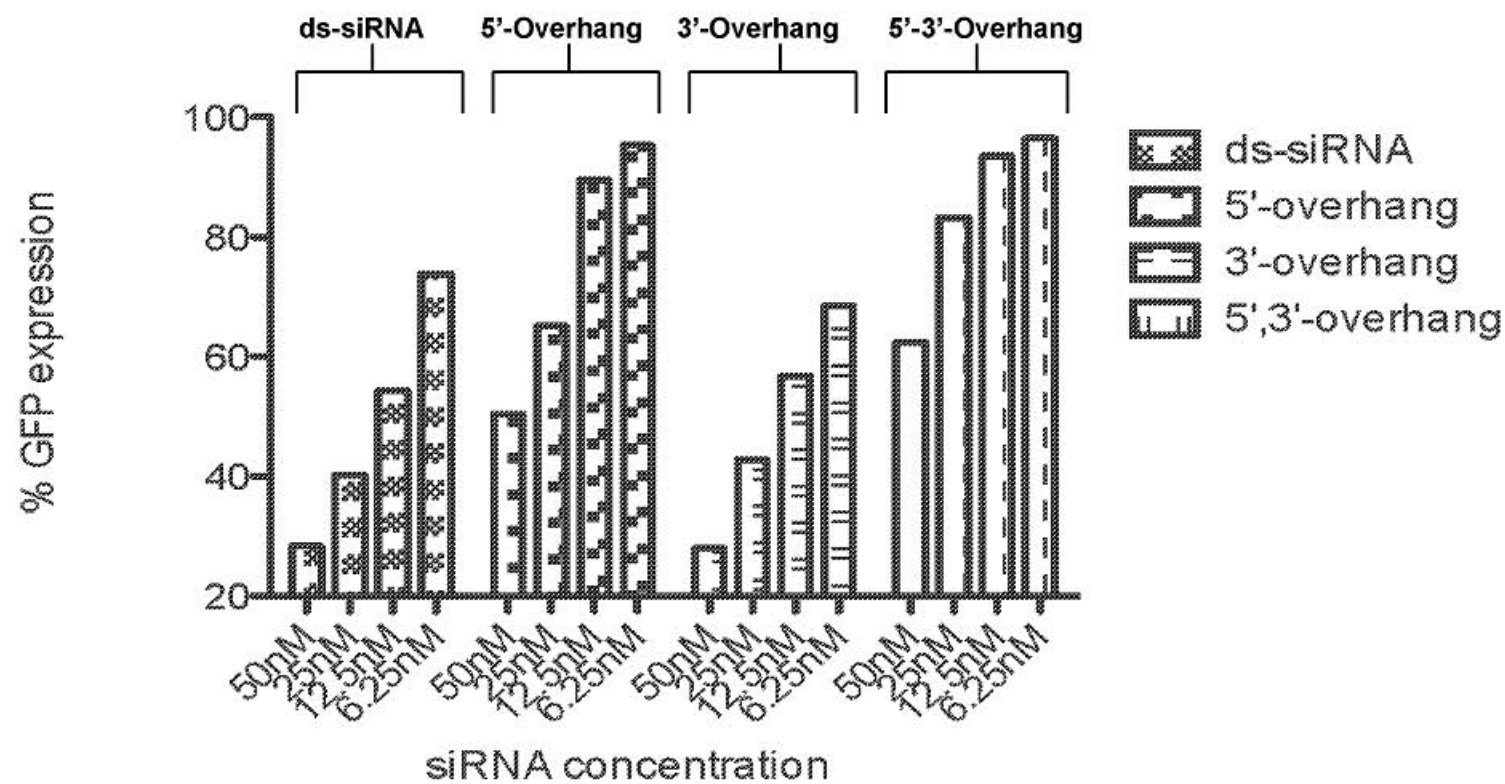


Fig. 30

S1: 5'-GTCTGAGGCAGTTGAG**AG**ATCTCGAACATTCC-Overhang-3' (SEQ ID NO. 7)
 f¹ b¹

S2: 5'-TAAGTCTGAAGATCC**ATTT**ATCACCAGCTGCTGCACGCCATAGTAG**AC**GTATCACCTGTCC- Overhang -3' (SEQ ID NO. 8)
 b² c¹ f²

S3: 5'-AGCTACTTGCTACACG**AGG**ATCTTCAGACTTAGGAATGTT**CGAGATCA**
 a¹ b³

CATGCGAGGACTCGGTCCAATACCGTACTA**AC**GATTACAGATCAA- Overhang -3' (SEQ ID NO. 9)
 e¹ a²

S4: 5'-CAGCTGGTGATAAA**AC**GTGTAGCAAGTAGCTTTGATCTGTAATCG**ACT**CTACGGGAAGAGC- Overhang -3'
 c² a³ d¹

S5: 5'-ATGCCCATCCGGCTC**ACT**ACTATGGCGTGCAG- Overhang -3' (SEQ ID NO. 10)
 d² c³

S6: 5'-CGAGTCCTCGCATG**ACT**CAACTGCCTCAGACGGACAGGTGATACGA
 e² f³

GAGCCGGATGGGCATGCTCTTCCCGTAGAG**AC**GGTATTGGACATGAT- Overhang -3' (SEQ ID NO. 11)
 d³ e³

Fig. 31

Preparing 6 Nick Tetrahedral

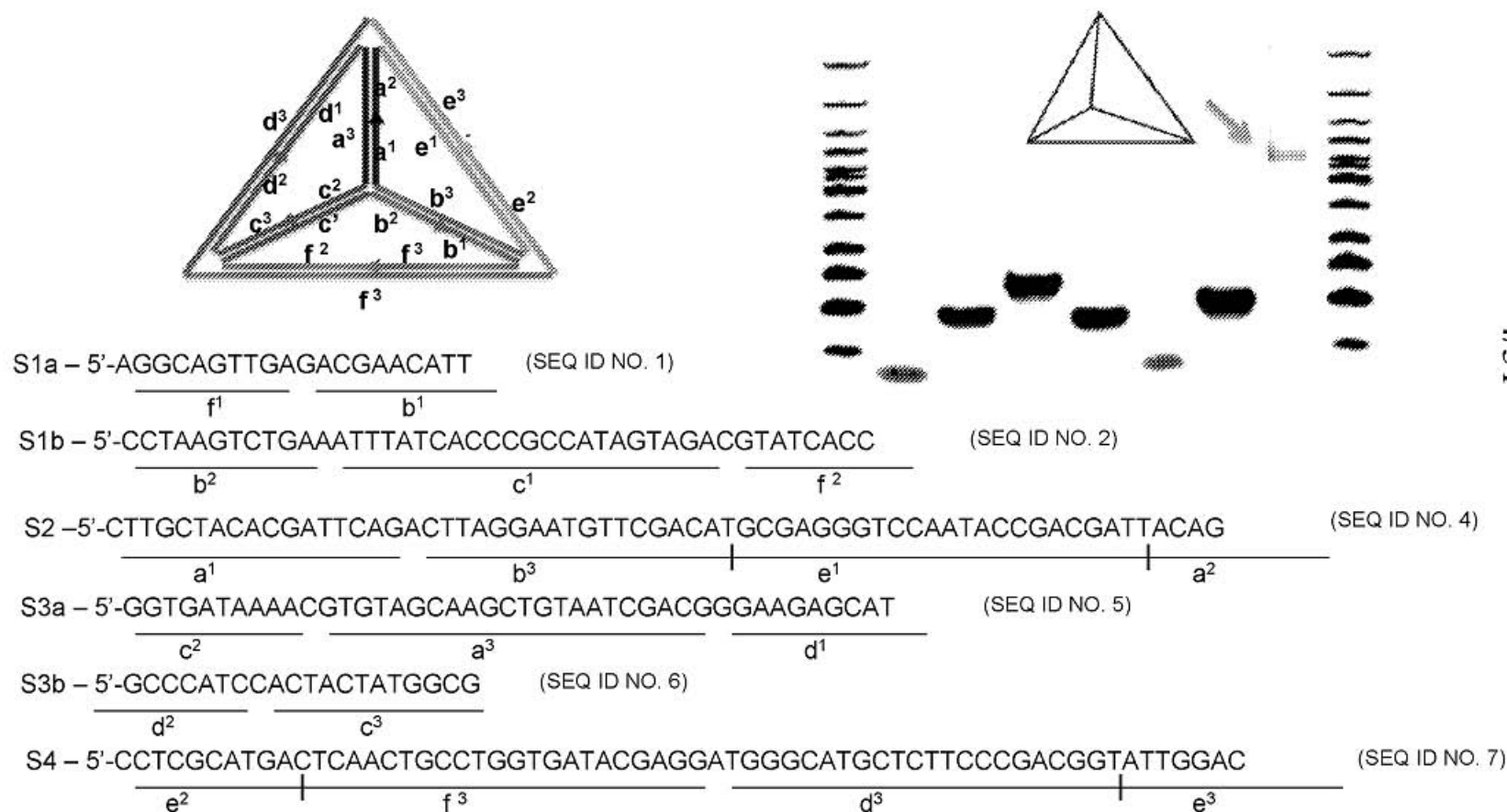


Fig. 4

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DNA Tetrahedron with siRNA

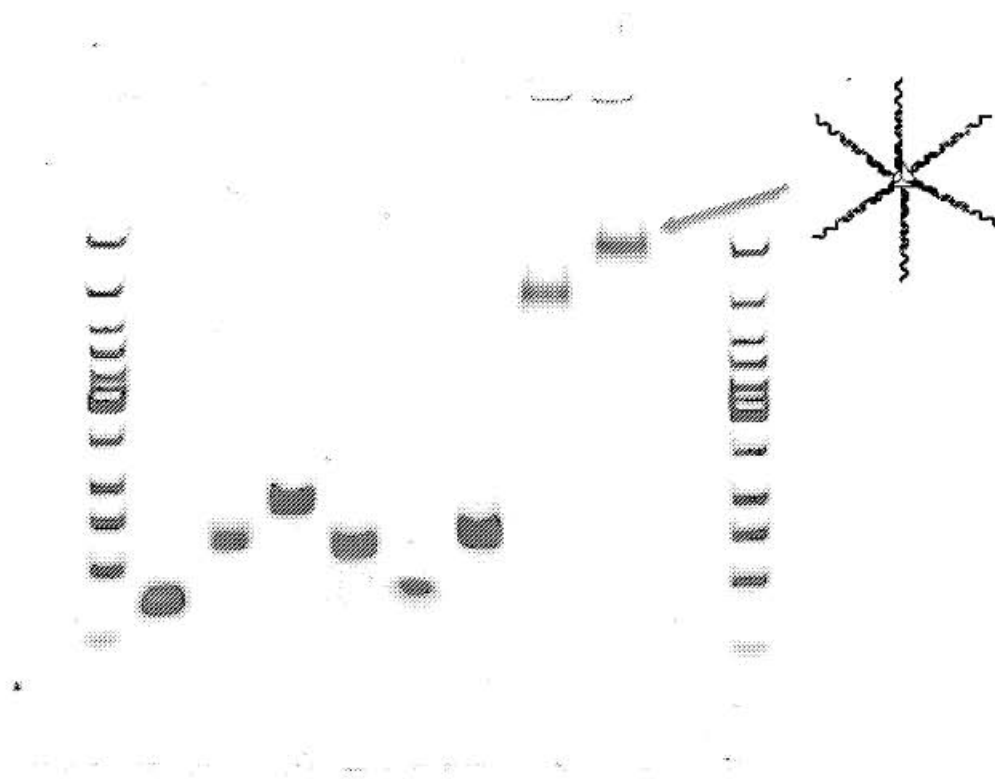


Fig. 5

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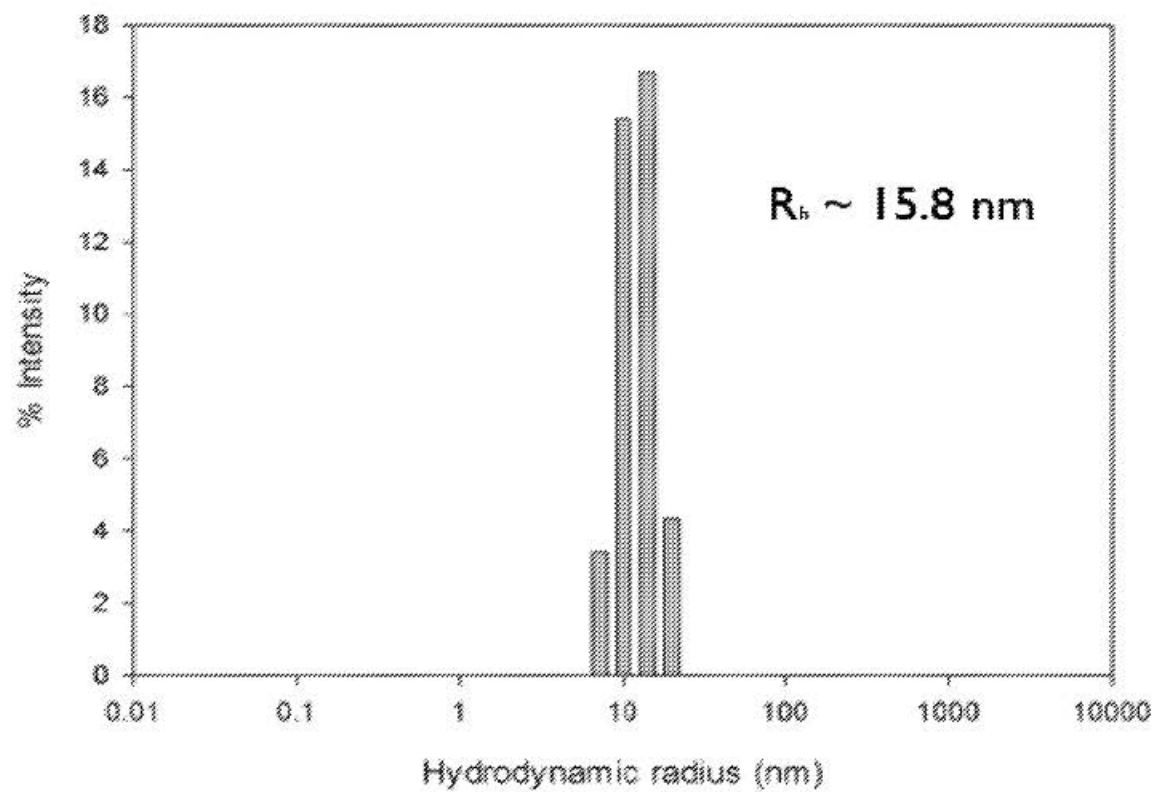


Fig. 6

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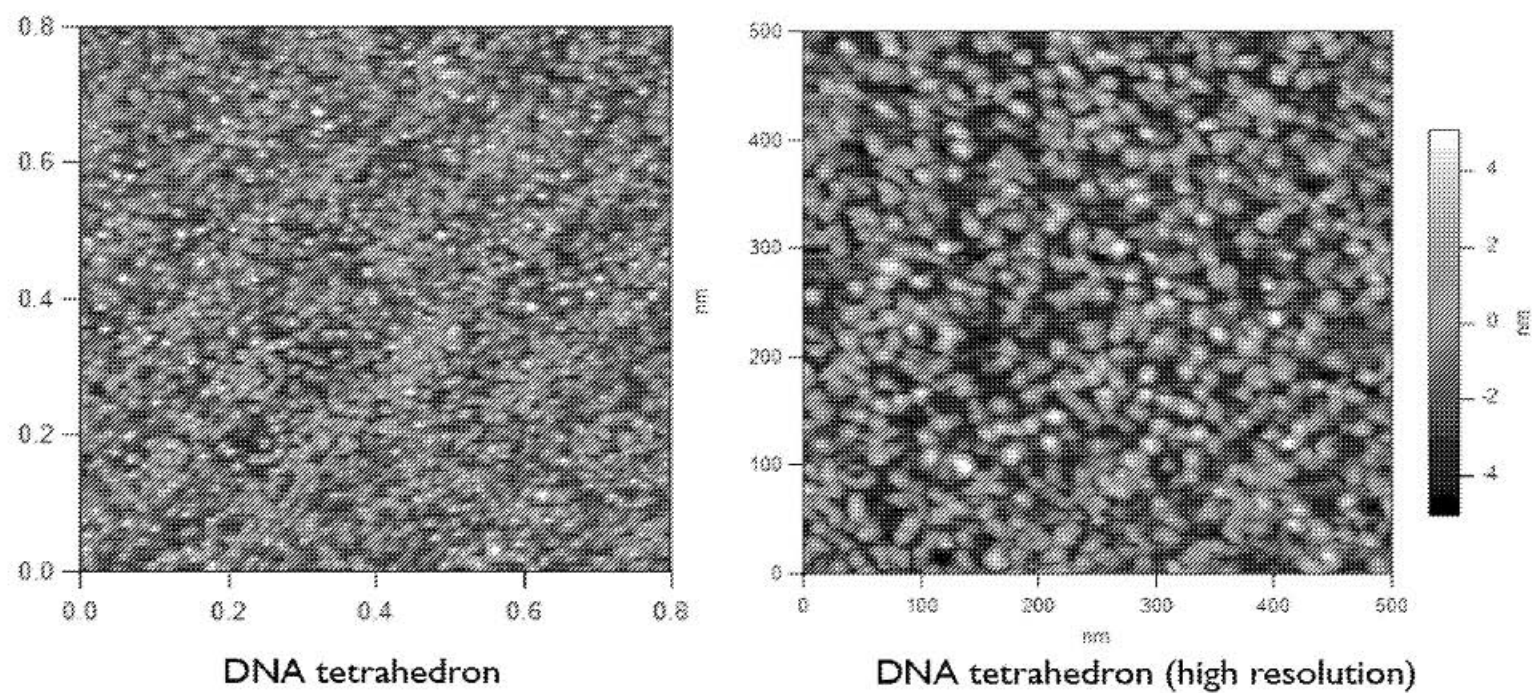


Fig. 7

- To facilitate intracellular delivery of DNA/RNA tetrahedron particles, conjugation of cell penetrating peptides were investigated.
- In addition to non-targeted approach, folate receptor mediated uptake was also investigated

List of cationic peptides:

1. HpH-1: YARVRRRGPRRGGC
2. Penetratin: RQIIWFQNRRMKWKK
3. HP4: RRRRPRTTTRRR
4. TAT: GRKKRRQRRRPPQ
5. MAP: KLALKLALKALKALKLA

Non-charged peptides from Manos:
23 different peptides

Receptor mediated delivery: Folate

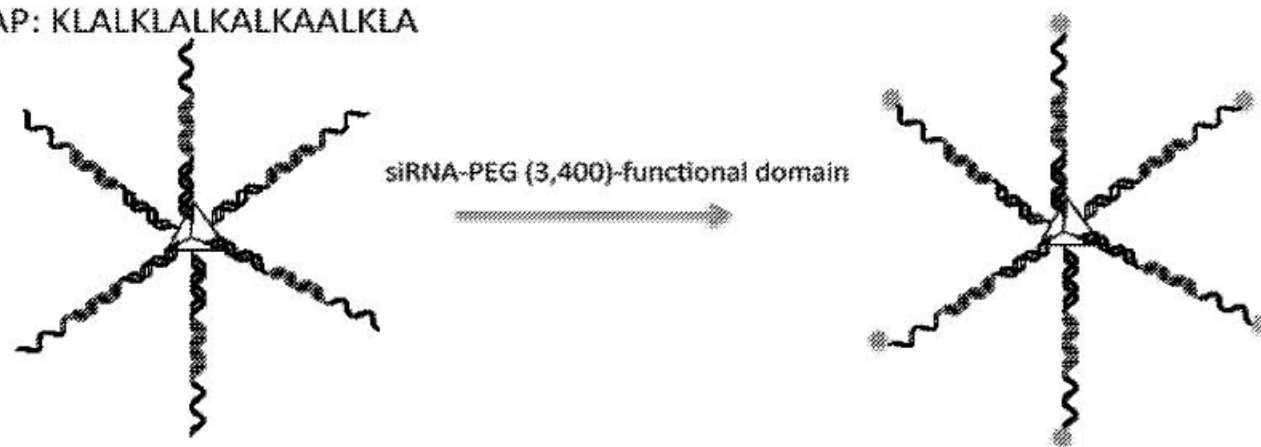


Fig. 8

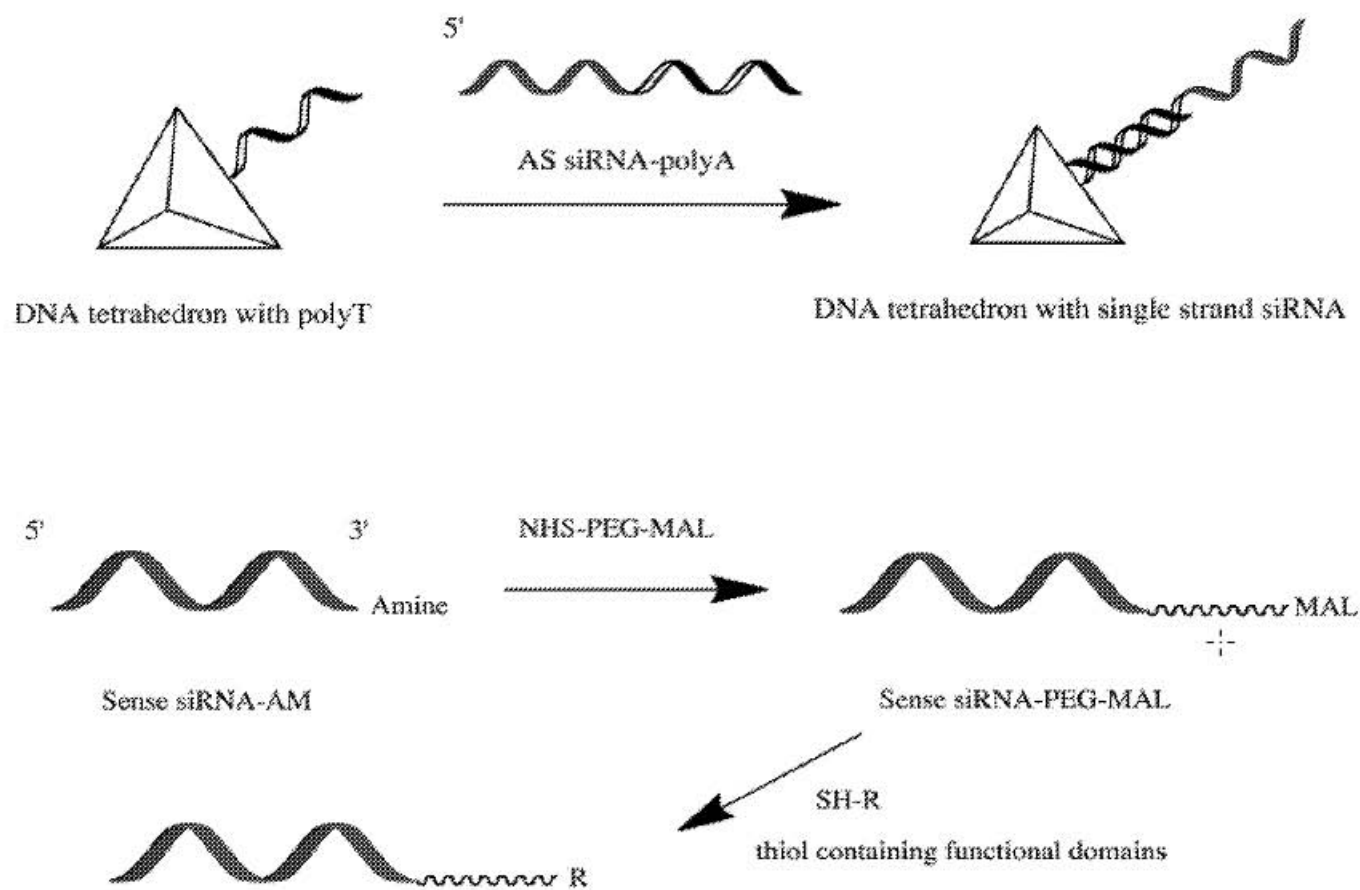


Fig. 9