Rapid development of caustic stable rAAV affinity resins

Novel affinity resins for AAV5 and AAV6 serotypes

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REPLIGEN

Caustic stability of AVIPure® AAV resins provides economic advantages for large scale purification of AAV

- NaOH stability enabling 100 cycles
- Consistent yield with elution at pH 3
- High DBC
- Excellent purity

The economic benefits of a reusable purification resin are realized with high mass productions of AAV

The dosage of AAV in clinical trials varies over 7 orders of magnitude!

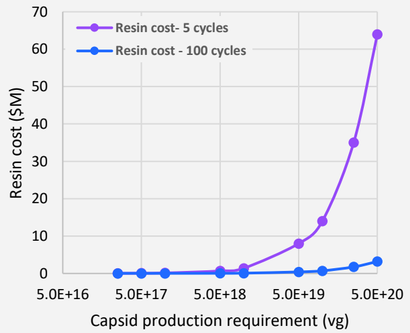
- Targeted AAV administration: 5.8 E+9 – 7.5 E+15 vg/dose
- Systemic AAV administration: 3.5 E+13 – 1.5 E+17 vg/dose
- A typical bioreactor titer is 3 E+14 vg/L
  - *A single dose can require a 500 L bioreactor!*

Cost modelling assumptions

- Capsids loaded to 1E+17 vp/L
  - 100 CV for typical reactor titer
- Average resin price $20K/L

Conclusions

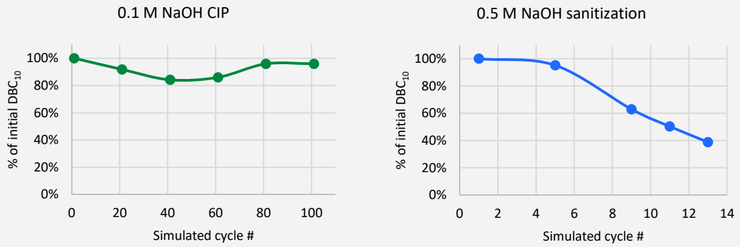
- For clinical indications requiring systemic administration serving > 1000 patients, cost savings of a reusable resin are in $M/yr



AVIPure® AAV5 retains high capacity after prolonged exposure to NaOH

To evaluate the stability of AVIPure® AAV5, DBC_{10} was measured before and after soaking the resin in 0.1 or 0.5 M NaOH for several hours

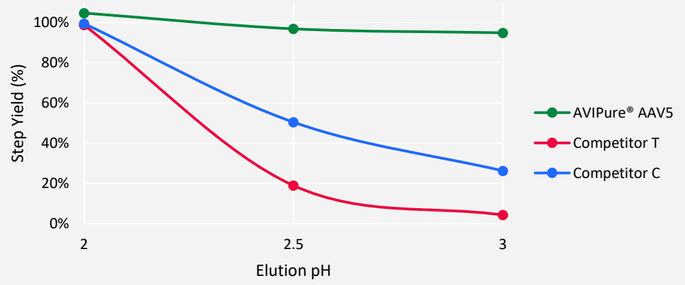
- 0.1 M NaOH simulated CIP cycle = 15 minutes
- 0.5 M NaOH simulated sanitization cycle = 30 minutes



AVIPure® AAV5 has excellent yield at pH ≤3

Purification runs were performed by challenging AVIPure® AAV5 or commercial resins with 133 CV of AAV5 HCCF at 1.5E+12 vp/mL_{RES}.

- Resin was loaded at 1 min RT and eluted at 4 min RT
- Elution buffer was 100 mM glycine, 150 mM NaCl, pH 2, 2.5 or 3

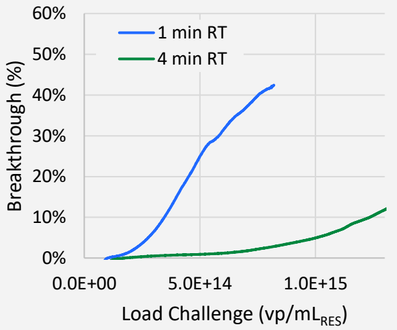


AVIPure® AAV5 has high capacity at short and long residence time

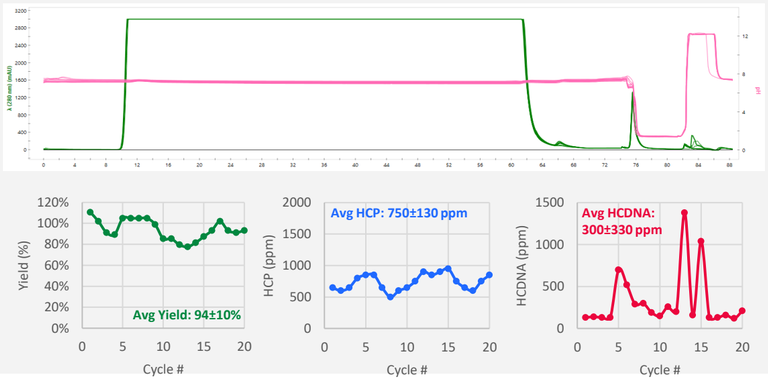
Dynamic binding capacity was measured at 1- and 4-min residence time:

- CV: 0.98 mL (0.5 x 5)
- 1 min RT challenge: 5.0E+12 vp/mL
  - 200 CV
- 5 min RT challenge: 1.13 vp/mL
  - 150 CV

Residence time	DBC_{10} (vp/mL_{RES})
1 min	3.5E+14
4 min	1.2E+15



AVIPure® AAV5 demonstrates consistent yield and purity over 20 purification cycles



Summary

AVIPure® capture resins for purification of AAV2, 5, 6, 8, and 9 are available today. High caustic stability and excellent yield at mild pH are key performance features.

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