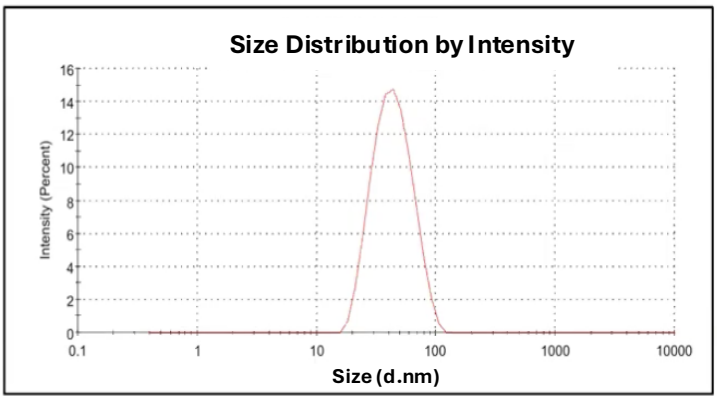
Paretor
155 Arlington St
Watertown, MA 02478

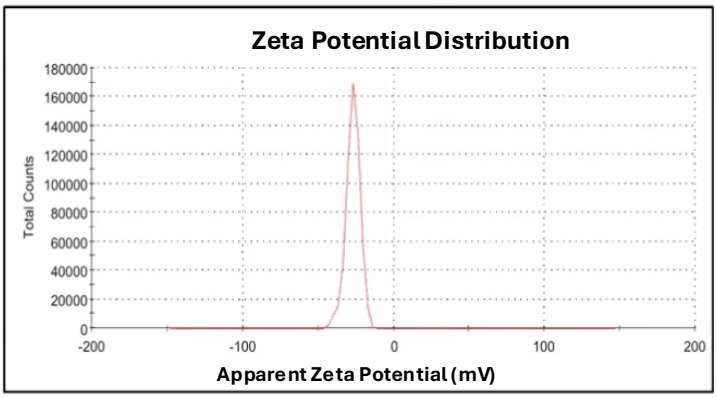
ETAERION™

Non-crystalline colloidal nanoparticles

Dynamic light scattering experiments show a single peak with normal distribution*



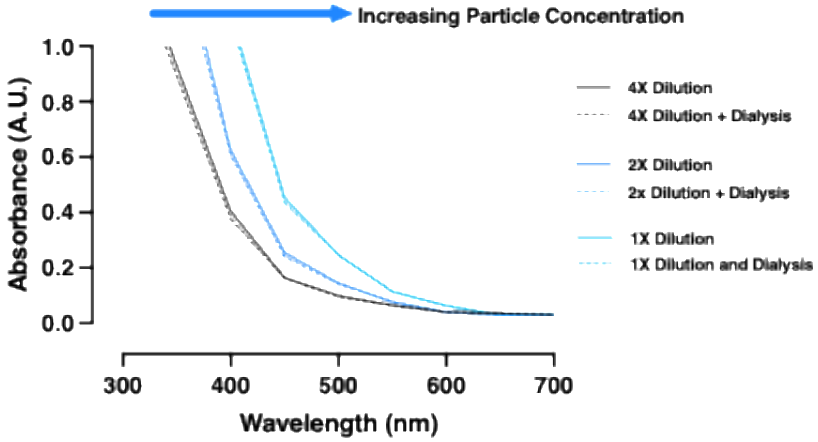
This is a single peak with a negative charge*



*Crude particles taken directly from the reactor

- Particles are uniform in size and charge
- Particles are not magnetic
- Straightforward to modify post-synthesis

Preservation of ETAERION™ Optical Profile with Dialysis



Interpretation: ETAERION™ remains structurally intact and does not release diffusible iron under buffer exchange conditions.

Dialysis against PBS does not alter the absorbance profile, indicating the signal is dominated by particle-associated iron and diffusible iron species are minimal under these conditions. Data suggest ETAERION™ remains structurally intact and does not release diffusible iron under buffer exchange conditions. Data also suggest there are minimal free iron residuals present post synthesis. Absorbance scales with particle concentration.

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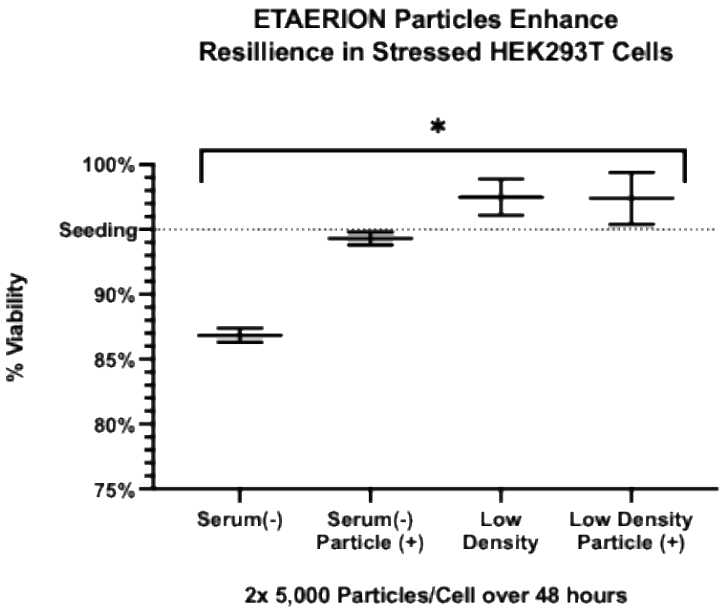
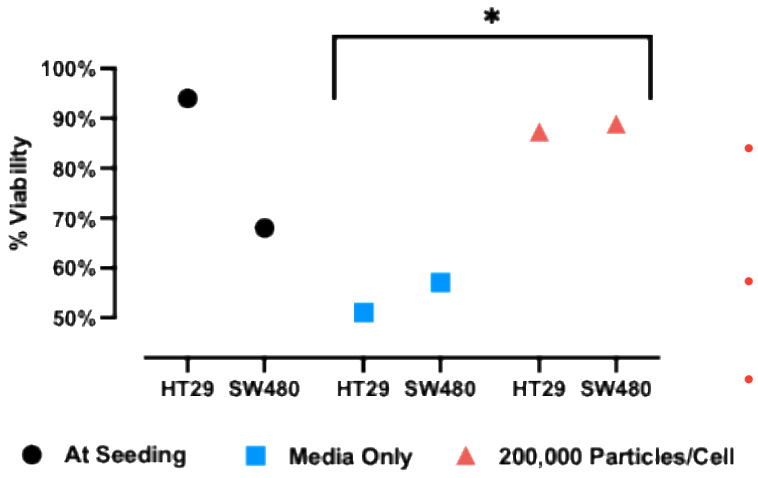
ETAERION™ improves how cells respond to high acute stress



- When serum-starved HEK293 cells are treated with 5,000 particles/cell (every 24 hours for 48 hours,) viability increases
- ETAERION™ particles do not appear to have an effect on cells seeded at low density, suggesting that increased viability is affected by the nature/severity of cell stress

An ordinary one-way ANOVA was performed to compare HEK293T cell viability across four treatment conditions (n = 8 total). A significant difference among group means was observed ($F(3,4) = 15.36$, $p = 0.0116$), indicating that treatment condition significantly affected cell viability. The model explained a large proportion of the variance ($R^2 = 0.92$).Variance across groups was not homogeneous, as indicated by a significant Brown–Forsythe test ($p < 0.0001$), suggesting that treatment effects differ not only in mean viability but also in variability. These results support a strong, condition-dependent effect of ETAERION exposure on cell viability under stress, consistent with a non-uniform, state-dependent biological response.

Interpretation: ETAERION™ improves viability selectively under stress conditions rather than acting as a universal enhance



- When HT29 and SW480 cells are treated with 200,000 particles/cell (every 24 hours for 48 hours) viability increases
- Data confirm preservation of viability without driving cell growth across multiple cell lines
- Viability is shown at seeding (black circles), after 48 hours in with media alone (blue squares), after 48 hours with ETAERION™ (red triangles)

Paired two-tailed t-test comparing C002-treated cells to media-only controls across matched colorectal cancer cell lines (HT29, SW480). C002 exposure resulted in a significant increase in viability (mean difference = +34%), $p = 0.041$ (exploratory analysis, n = 2 paired lines).

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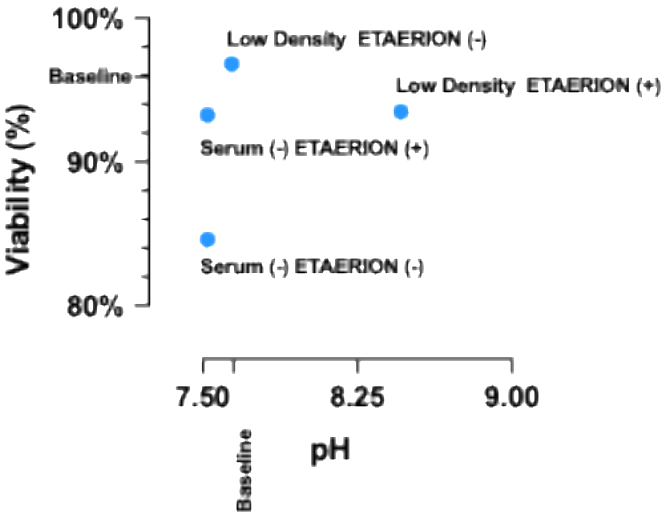
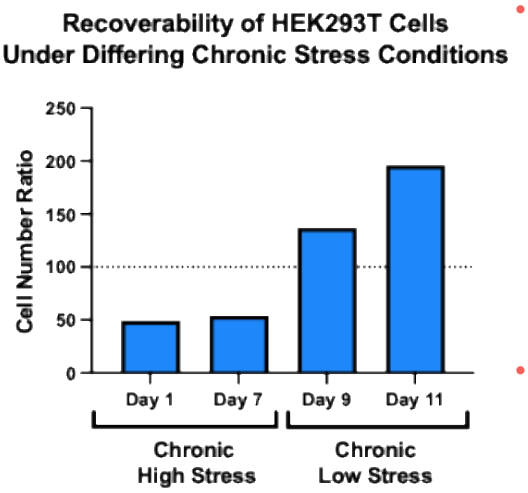
ETAERION™ reduces media acidification in HEK293 cells in acute settings (48 hours)



- Serum-starved cells show increased viability when exposed to ETAERION™ (5,000 particles per cell over 48 hours)
  - The magnitude of the effect is reduced relative to prior experiments, consistent with lower particle dose and higher baseline viability
- In low-density conditions, ETAERION™ does not significantly alter viability but increases media pH, indicating reduced acidification

Interpretation: ETAERION™ modulates extracellular pH, with downstream effects on viability dependent on stress context (impact is greater for low-stress conditions; i.e., low-density plating)



- HEK293T cells with or without 5,000 particles/cell of ETAERION™ were serum starved for seven days. Viability at each time point is shown as a ratio of the number viable cells in the ETAERION™ cultures to the number of viable cells in the serum-only cultures
  - Viabiilty on Day 1 and Day 7 suggest that ETAERION™ confers a disadvantage to cells under chronic high-stress conditions
- On day 7, cells were passed and supplied with normal media
  - At Days 9 and 11, restoration of viability is enhanced for ETAERION™-containing cultures. This crossover behavior is consistent with a state-dependent response

Interpretation: ETAERION™ does not universally enhance growth, but instead modulates system performance within a defined window of viability, where it can enhance recovery following a transition out of chronic high stress environments

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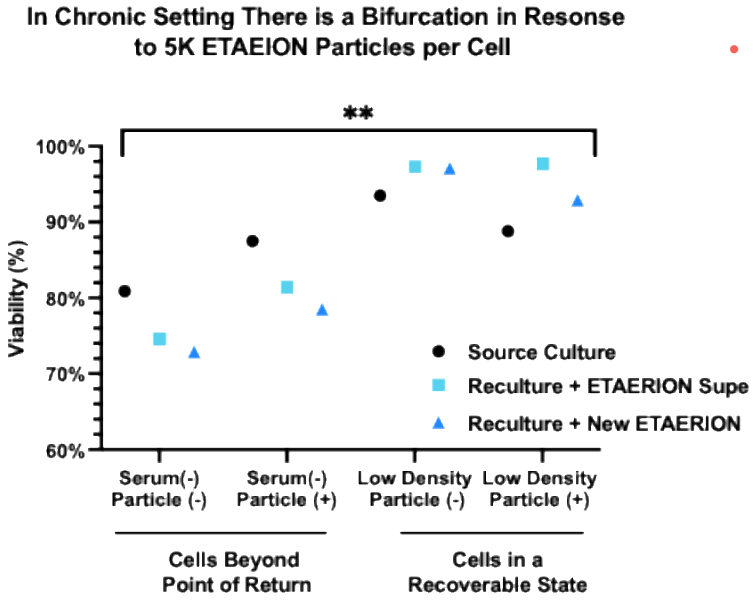
Under Chronic Stress Conditions (96 hours) there is a bifurcated, cell-stress threshold-based response to EATERION™



Two-way ANOVA (ordinary, α = 0.05) was used to assess the effects of culture condition (row factor) and treatment (column factor) on cell viability. A significant main effect of culture condition was observed ($F(3,6) = 13.79$, $p = 0.0042$), accounting for ~86% of total variance, indicating that baseline stress state strongly determines viability. No significant main effect of treatment alone was detected ($F(2,6) = 0.40$, $p = 0.687$), suggesting ETAERION does not uniformly alter viability across all conditions. Residual variance was low (MS = 18.6), consistent with a structured, condition-dependent response. These data support a state-dependent biological effect, in which ETAERION's impact emerges only within specific stress regimes rather than as a global viability enhancer.

- A source culture of HK293 cells was grown for 48 hours in one of four conditions (either serum-starved or low-density conditions with or without particle). Black circles show viability at 48 hours
  - At 48 hours, cells in each condition were re-cultured with either new ETAERION™ (square) or supernatant from the low-density + particle source culture (triangles)
  - When cells were re-cultured, stress conditions (serum(-) or low-density plating) were maintained
- 48 hours following initiation of re-culture, viability was measured
  - In serum-starved conditions, ETAERION™ reduces viability, indicating a reversal of effect under more severe stress
  - ETAERION™ increases viability in low-density (recoverable) cultures
- Response to conditioned supernatant suggests involvement of soluble or environment-mediated effects

Interpretation: These results support a model in which ETAERION™ modulates cellular outcomes in a context-dependent manner rather than as a universal viability enhancer. In addition, results suggest a physicochemical environmental effect may contribute to ETAERION™ activity.

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ETAERION™ Improves recoverability of cells following freeze-thaw

- Pre-conditioning cells with ETAERION™ 48 hours prior to freezing improves post-thaw recoverability relative to untreated controls
- Inclusion of ETAERION™ in freeze media does not improve outcomes and may transiently reduce viability immediately after thaw
- Addition of ETAERION™ post-thaw enhances recovery, with the greatest benefit observed in cells pre-conditioned prior to freezing
- The strongest recoverability is observed when ETAERION™ is applied both before freezing and after thaw, indicating a staged effect on cellular resilience and recovery

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