

**DOWNSTREAM IMPROVEMENT FOR RECOMBINANT ADENO-ASSOCIATED VIRUSES (RAAV)
PRODUCED IN ICCELLIS NANO 4 M² ADHERENT BIOREACTOR**

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In the clarification of recombinant adeno-associated virus cell culture (rAAV), unwanted cellular material is separated from the vector to increase its purity and enable further downstream processing. In industrial settings, primary clarification with depth filters is used to remove larger particles, such as cells and cellular debris originating from cell lysis and benzonase treatment. To reduce the challenge on the downstream process a clarification step that can eliminate these contaminants with minimal rAAV loss is highly desirable for robust GMP manufacture. We are working towards improving the clarification and downstream steps for rAAV5, 9 and other rAAV subtypes. We produced rAAV on the iCELLis Nano 4 m² adherent bioreactor with 8 L media. At the point of harvest, the cells were lysed and were treated with benzonase. The upstream feed was assessed for turbidity and subsequently processed and concentrated by depth filtration and Tangential Flow Filtration (TFF) and the reduction in turbidity determined.