

## A sticky situation: New insight into manufacturing safer biopharmaceuticals at lower cost

January 20 2016



Credit: AI-generated image (disclaimer)

Monoclonal antibodies are an important new class of drugs to treat cancer, heart disease and a range of other conditions. However, their production in mammalian cells introduces a large number of contaminants that are difficult to remove during purification. Now, by



looking at how antibodies change chemically during purification, A\*STAR scientists have identified a better way to eliminate contaminants.

Protein A affinity chromatography is a technique that has dominated the field of antibody purification for the past 20 years, thanks to its remarkable ability to selectively bind to Immunoglobulin G (IgG). However, the purified antibody always contains more contaminants than it should. Previous studies compared IgG characteristics before and after protein A, and did not reveal why these contaminants persisted, but the technique still worked so well that there seemed little need to dig deeper.

Pete Gagnon and his team from the A\*STAR Bioprocessing Technology Institute thought there was more to the question and decided to look more closely at what was happening to the antibody during the purification process, especially during elution when IgG is separated from protein A. Their findings came as a surprise.

"The antibodies became chemically 'sticky' under these conditions", says Gagnon, "worse than that—they stuck to contaminants, and carried them along with them."

Nothing could be done about the chemical conditions that cause the IgG to become sticky. But the team found a clever way out of this sticky situation—they discovered a class of contaminants called chromatin heteroaggregates that adhere to protein A even more strongly than IgG. "Chromatin is the operative element in a covert system for smuggling contaminants through purification methods—remove the chromatin in advance and there is nothing for the IgG to stick to," says Gagnon.

By removing <u>chromatin</u> in advance, the team was able to achieve better purification with just protein A than most licensed manufacturing procedures can achieve with <u>protein</u> A and two additional steps. Gagnon



cautions that this does not mean that purification of therapeutic <u>antibodies</u> can done with just one step, but it does mean that higher purity IgG can be achieved faster with less work and fewer materials.

Gagnon concludes: "Big improvements in process economics often demand compromises in performance, but here we have a situation where both economics and purification performance are improved. It's all upside."

**More information:** Pete Gagnon et al. Non-immunospecific association of immunoglobulin G with chromatin during elution from protein A inflates host contamination, aggregate content, and antibody loss, *Journal of Chromatography A* (2015). DOI: 10.1016/j.chroma.2015.07.017

Provided by Agency for Science, Technology and Research (A\*STAR), Singapore

Citation: A sticky situation: New insight into manufacturing safer biopharmaceuticals at lower cost (2016, January 20) retrieved 26 June 2024 from <u>https://phys.org/news/2016-01-sticky-situation-insight-safer-biopharmaceuticals.html</u>

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