# From Egg White to Bone: Albumin-based Scaffolds for Endochondral Cartilage Engineering

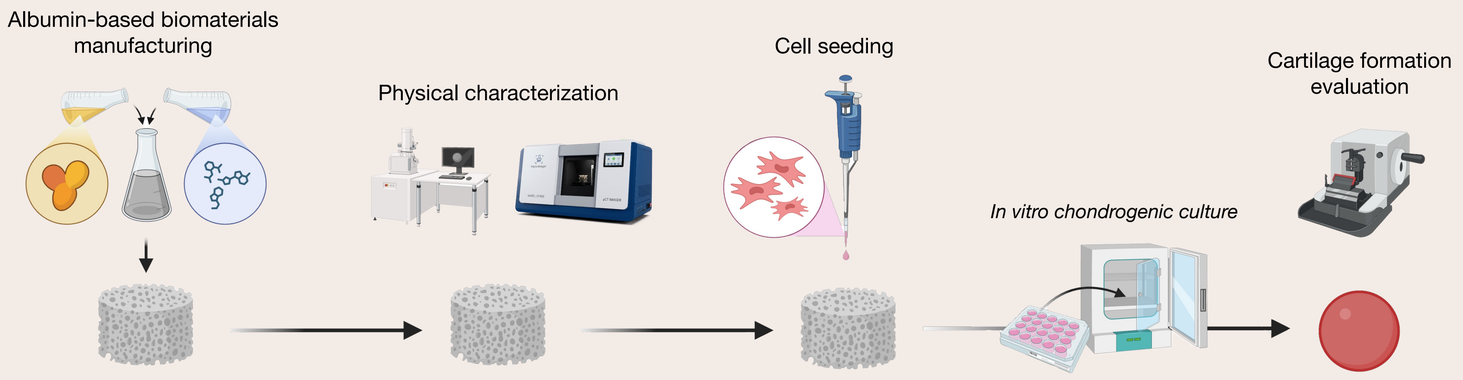
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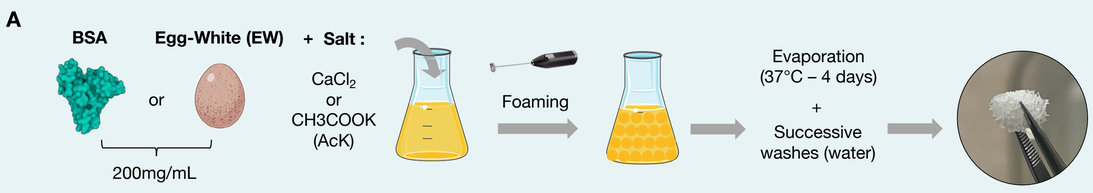
## Abstract

In this work, porous albumin-based scaffolds were fabricated from bovine serum albumin (BSA) or egg-white (EW) proteins through a salt-assisted foaming process. Physical characterization showed that salt formulation strongly influences pore size distribution and accessibility. When seeded with adipose-derived stromal cells (ASCs) and cultured in chondrogenic conditions for up to 8 weeks, albumin-based scaffolds supported robust cartilage formation and yielded larger tissues than collagen controls, while persisting within the constructs. These results highlight albumin-based biomaterials as a versatile, natural and cost-effective alternative to collagen for cartilage tissue engineering applications.

## Study Design




## 1 - Material manufacturing process




B

| Name | Material | Salt (concentration) |
|---|---|---|
| BSA $CaCl_2$ | Bovine Serum Albumin | Calcium chloride (2M) |
| BSA AcK | Bovine Serum Albumin | Potassium acetate (7,5M) |
| EW AcK | Egg White | Potassium acetate (7,5M) |
| Collagen | UltraFoam™ Collagen | X |

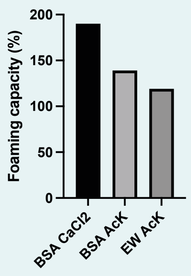



**Figure 1. Generation of albumin-based materials. (A)** Material formulation by salt-assisted compaction : bovine serum albumin (BSA) or egg-white (EW) proteins were solubilised into an acetate buffer (pH=6). Protein solutions were mixed with various salts and stirred to create foam which was transferred into silicone moulds and dried at 37 °C for 4 days. Resulting porous materials were washed with water and stored in 20% ethanol until use. **(B)** Composition of the tested albumin-based materials (yellow) is detailed in the table; their biological properties were compared with a standard collagen scaffold (blue). **(C)** Foaming capacity of albumin-based materials, calculated as % volume increase after stirring: (V2–V1)/V1×100, where V1 and V2 are the volumes before and after stirring, respectively.

## 2 - Physical characterization

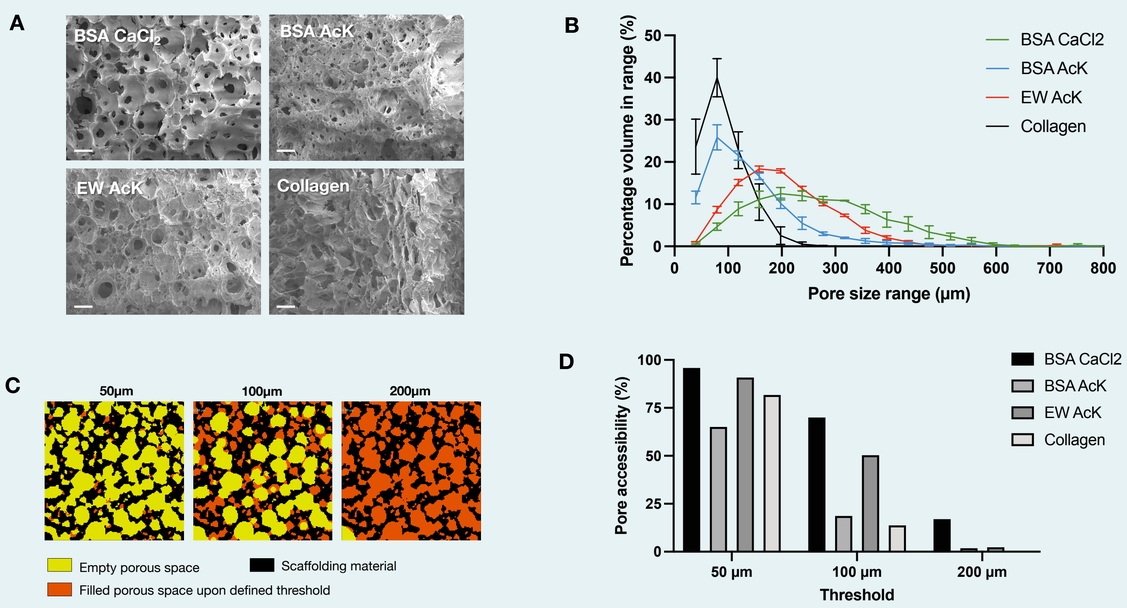



**Figure 2. Material formulation drives scaffolds porosity. (A)** SEM images of albumin-based and collagen scaffolds (60X). Scale bar : 200µm. **(B)** Pore size distribution of albumin-based and collagen sponges quantified after micro-CT imaging. **(C)** Pore accessibility was assessed by generating a thickness map of the pore network and testing whether spheres of defined diameters could fit within the available space. The analysis was repeated using three thresholds, corresponding to 50, 100, and 200µm, and the resulting maps show accessible (yellow) versus inaccessible (red) regions in the scaffold. **(D)** Pore accessibility was quantified as the percentage of the total pore volume accessible at each threshold, and compared across the different materials. It reflects how scaffold composition affects the fraction of the pore network that remains accessible for cells seeded onto it for tissue engineering applications.

## 3 - In vitro cartilage engineering







**Figure 3. Albumin-based scaffolds support chondrogenic differentiation of adipose stromal cells (ASCs). (A)** Experimental workflow: ASCs were obtained from cultured stromal vascular fraction (SVF) cells isolated from human adipose tissue, then seeded on albumin-based or collagen scaffolds. Constructs were cultured in chondrogenic medium for 4 or 8 weeks. **(B)** Safranin-O staining of cartilage pellets cultured for 4 **(a–d)** and 8 weeks **(e–h)** with: collagen **(a,e)**, EW AcK **(b,f)**, BSA $CaCl_2$ **(c,g)**, and BSA AcK **(d,h)**. Scale bar: 1mm. **(C–D)** Albumin-based cartilage showed a similar GAG/DNA ratio—indicative of cartilage maturation—to collagen-derived constructs after **(C)** 4 weeks (BSA AcK only) and **(D)** 8 weeks (all materials) (n=3). **(E)** Quantification from Safranin-O images using QuPath: **(a)** representative image, **(b)** pellet area, **(c)** remaining scaffold area , and **(d)** surrounding cartilage area in constructs cultured for 4 and 8 weeks (n=3). Because all albumin-based materials behaved similarly, only EW AcK results are shown here, for simplicity reasons. EW AcK-derived cartilage pellets were larger than collagen-based counterparts, likely due to scaffold persistence after 8 weeks. Although cartilage area was similar at 4 weeks, EW AcK sponges enabled a greater cartilage area than collagen at 8 weeks. Data are shown as mean ± SD. Statistical significance: *p<0.05, **p<0.01, ***p<0.001, ns = not significant.

## Conclusions

**1.** Albumin-based sponges can be generated from various sources and different salt formulations with a simple yet robust protocol.

**2.** Albumin proteins and salt combinations strongly influences scaffold pore size distribution and accessibility for cells.

**3a.** They support chondrogenic differentiation of ASCs and enable the formation of larger cartilage organoids compared to collagen.

**3b.** Unlike collagen scaffolds, albumin-based materials persist during *in vitro* cartilage culture, within the construct.

**Perspectives**

Endochondral ossification (ECO) is the process by which hypertrophic cartilage remodels into bone, with vascular ingrowth into the cartilage. Given albumin's pro-angiogenic properties, such new scaffolds are a promising alternative to collagen for skeletal repair.

Next, we will implant albumin-based hypertrophic cartilage constructs *in vivo* to assess ECO and scaffold remodelling, and explore hybrid albumin-collagen scaffolds with potentially improved properties.

## References

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