



Amnio2x is a multipurpose, growth factor supplemented, frozen allograft of placental origin

## The Exosome Revolution in Regenerative Medicine

DUNCAN ROSS PH.D.

**Amniotic fluid (AF)** has taken the regenerative medicine world by storm over the last decade. It contains a substantial number of growth factors and immune components that provide benefits to a myriad of patients for regenerative purposes. It is readily available, simple to acquire, and satisfies a multitude of indications for achieving human health and vitality. Taking full advantage of its features, Kimera Labs provides three amniotic fluid derived products with varying degrees of potency to support your needs in the practice of Regenerative Medicine.

### Key components of commercial AF include:

- Maternal Epithelial Cells
- DMSO
- Growth Factors
- Hyaluronic Acid
- Innate Immune Components: Defensins, etc.
- Exosomes

### *Maternal Epithelial Cells*

One of the myths of amniotic fluid shared across the health industry is that amniotic fluid contains 'stem cells' and that these are responsible for the benefits seen in the use of AF. This is simply a myth. The major cellular component of amniotic fluid is the mother's epithelial cells that slough off into the fluid. In fact, when no infant is present, you can identify the same cells by observing the menses of a female patient. The majority of scientific peer-reviewed articles that discuss amniotic fluid derived stem cells are from early term amniocentesis, prior to the hardening of the outer layer of the child's skin. In a poster presented at the 2016 American Association of Tissue Banks conference in New Orleans, LA, 200 ml of fresh C-section derived amniotic fluid was taken directly from the delivery room to the lab and immediately cultured. In 200ml of **FRESH AF**, 40 mesenchymal stem cell colonies were identified. That is less than 1 MSC per ml, using fresh, non-cryopreserved fluid. Furthermore, these third-party cells would be rejected by the patient's immune systems.

### *DMSO*

Dimethyl Sulfoxide is a cryo-preservant included in amniotic fluid ostensibly to protect the stem cells discussed in the previous paragraph. The use of DMSO requires that it be used at a 1:1 ratio with the fluid being preserved. In practice, this reduces the amount of amniotic fluid present by half. Further, when cells are taken out of cryopreservation 20-30% of the cells are lost due to the toxic nature of DMSO. Indeed, it is well known that if cells are left in DMSO at room temperature, 100% of the cells will be destroyed. DMSO requires careful handling at 4°C to not be lethal.

### *Growth Factors*

Amniotic fluid has been shown to contain many growth factors including the following: TIMP-2, HGF, TIMP-3, IGF-2, IL-6, GRO-ALPHA, TGF-β3, IL-1Rα, TIMP-4, MCP-1, EGF, TGF-α.<sup>1</sup>

### *Hyaluronic Acid*

A major component of Amniotic fluid, HA cushions the fetus in the womb and can provide that homologous function when used for orthopedic uses.<sup>2</sup>

### *Innate Immune Components*

It is vital that the womb remains a sterile environment for the fetus. Amniotic fluid is comprised of hundreds of proteins, calprotectin and permeability-increasing proteins that can provide an innate immune solution to invading pathogens. These proteins include α-defensins



[HNp1-3], lactoferrin, lysozyme, bactericidal/permeability-increasing protein, calprotectin, secretory leukocyte protease inhibitor, psoriasin [S100A7], and a cathelicidin [LL-37] 3,4,5 For this reason, the use of amniotic fluid in the surgical space is absolutely indicated as pathogen prophylaxis and is a boon to the field.

**Exosomes**

Exosomes are 100nm lipid vesicles that are secreted by most cell types. Indeed, besides hormones, growth factors and signaling proteins are usually secreted in these vesicles, allowing for their protection from proteases and facilitating uptake by target tissues. Exosomes are comprised of not only proteins but also messenger RNA and microRNA<sup>6</sup>. The uptake of the latter into the cytoplasm of the target cell can cause *new growth factor expression in older cells as well as modulate the expression of normal cell products*. While exosomes secreted by mesenchymal stem cells are currently a central topic of investigation<sup>7</sup>; epithelial cells<sup>8</sup>, dendritic cells<sup>9,10</sup>, B cells<sup>11</sup>, T cells<sup>12</sup>, and mast cells<sup>13,14</sup> all secrete these vesicles. Exosomes have been found in plasma<sup>15,16</sup>, urine<sup>17</sup>, breast milk<sup>18</sup>, saliva<sup>19</sup>, bronchoalveolar lavage<sup>20</sup>, and amniotic fluid<sup>21</sup>.

**We are the Exosome Experts**

By understanding how to isolate and concentrate exosomes, Kimera Labs has created an industry first

amniotic fluid product, **Amnio2x**, which provides all that amniotic fluid contains augmented with 2mg of placental exosomes per ml, allowing the clinician to achieve reproducible results that are more powerful than any product on the market today!

**Kimera Amnio Products**

**Amniotic Fluid**

A standard 1ml amniotic fluid that is cryo-preserved with DMSO as per the typical product on the market today. This product would contain live cells and has been tested for sterility. This product must be maintained cryopreserved at -80°c until use.

**Amnio2**

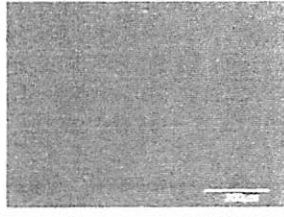
Amnio2 is offered in a 1ml and 2ml size. Amnio2 is pure amniotic fluid with no cells, DMSO, or requirements for cryo-preservation beyond normal freezer temperatures.

**Amnio2X**

Amnio2X is the first of its kind product that melds the benefits of amniotic fluid with a minimum of 1mg/ml of added growth factor rich exosome products. A thorough understanding of growth factor production and packaging process is required to formulate Amnio2X, a singularly powerful Regenerative Medicine product to achieve reproducible clinical results. Amnio2X is available in 1ml and 2ml sizes.

|                       |              |               |                |
|-----------------------|--------------|---------------|----------------|
|                       | <b>Amnio</b> | <b>Amnio2</b> | <b>Amnio2x</b> |
| <b>Live Cells</b>     | YES          | NO            | NO             |
| <b>DMSO</b>           | YES (500uI)  | NO            | NO             |
| <b>Amniotic Fluid</b> | 1/2X         | X (1ml)       | X (1ml)        |
| <b>HA</b>             | 1/2X         | X             | X              |
| <b>Exosomes</b>       | 1/2X         | X             | XXX            |

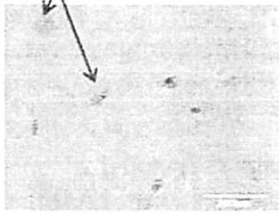
**Amnio2X™**  
Purified human amniotic fluid  
No Tissue Fragments No Cryopreservative



**Amnio2x provides:**

- 2X the growth factors
- 2X the cushioning
- 2X the anti-microbial peptides
- 2X the healing as the leading amniotic fluid products

**OrthoFlo™**  
Purified human amniotic fluid  
Viable cells No tissue fragments



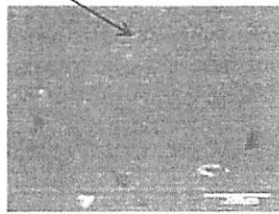
**BioDFactor®**  
Human amniotic fluid with tissue  
Few viable cells Tissue fragments



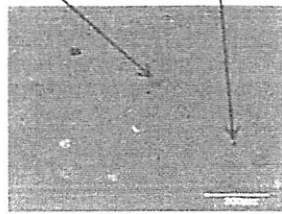
**Potential Clinical Applications:**

- Orthopedics
- Neurosurgery
- Spinal Surgery
- General Surgery
- Urology
- Erectile Dysfunction
- Wound Healing

**AmnioVisc™**  
Purified human amniotic fluid  
Viable cells No tissue fragments



**PalinGen® SportFlow**  
Human amniotic fluid with tissue  
Dead cells Tissue fragments



**PalinGen® Flow**  
Human amniotic fluid with tissue  
Dead cells Tissue fragments



**AlloGen®**  
Human amniotic fluid with tissue  
No intact cells Small particulate



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