How Wharton's Jelly Exerts Its Regenerative Effects

The science of WJ-MSC paracrine signaling

IN BRIEF

Wharton's Jelly is the soft tissue inside the umbilical cord. It contains one of the highest concentrations of mesenchymal stem cells found in any perinatal tissue.

These cells were once thought to work by turning into new tissue themselves. Current research points to a different mechanism: they release a mix of signaling molecules, called the secretome, that changes how nearby cells behave.

Laboratory evidence for those signaling effects is well documented. Human clinical evidence is still developing and varies by condition.

Introduction

Wharton's Jelly (WJ) is the soft, gelatinous connective tissue found inside the umbilical cord, surrounding the umbilical blood vessels. It is a rich source of mesenchymal stem cells (MSCs), and research suggests it contains one of the highest concentrations of MSCs found in any perinatal tissue.[1] For years, the prevailing view was that these cells aided healing by differentiating into new tissue directly. More recent research points to a different and arguably more important mechanism: paracrine signaling.

What paracrine signaling means

Paracrine means, simply, nearby cell to cell. Rather than replacing damaged cells directly, WJ-MSCs release a collection of bioactive molecules, collectively called the secretome, into the surrounding environment. The secretome acts as a set of chemical instructions that influence the behavior of neighboring cells.[1] It has two broad components:

- **Soluble factors.** Growth factors, cytokines, chemokines and enzymes released directly into the surrounding tissue.[1]
- **Extracellular vesicles.** Including exosomes, membrane-bound packages roughly 30 to 150 nanometers across that carry proteins, lipids and genetic material such as microRNA to target cells.[1]

What the secretome appears to do

A 2023 peer-reviewed review in Frontiers in Cell and Developmental Biology describes several biological effects studied in the WJ-MSC secretome:[1]

- **Immunomodulation.** Influencing how immune cells respond, generally in an anti-inflammatory direction.
- **Tissue repair signaling.** Promoting processes involved in wound healing and tissue remodeling.
- **Anti-fibrotic activity.** Laboratory and early clinical research has explored whether the secretome can limit excess scar tissue formation in organs such as the liver and lungs.
- **Angiogenesis support.** Signaling associated with the formation of new blood vessels, which is important for healing tissue.

Evidence status

Evidence status	What this means
Established	The existence of the WJ-MSC secretome, its general composition, and its immunomodulatory activity in laboratory and animal models is well documented across many independent studies.[1]
Emerging	Small clinical studies and case reports have explored WJ-MSCs and their secretome in conditions such as graft-versus-host disease, diabetes, and COVID-19 related lung inflammation, with encouraging but limited results.[1]
Limited	Large, high-quality randomized controlled trials confirming clinical efficacy for most specific human indications are still lacking, and long-term safety data in large patient populations remains limited.[1] Laboratory and small-study findings should not be read as proof that a specific clinical outcome is assured.

Key points

- ▪ WJ-MSCs are understood to work mainly through their secretome, not primarily by becoming new tissue.
- ▪ The secretome contains both soluble factors and extracellular vesicles such as exosomes.
- ▪ Documented laboratory effects include immunomodulation, tissue repair signaling, anti-fibrotic activity and angiogenesis support.
- ▪ Human clinical evidence is still developing and varies significantly by condition.

Source verification

Claim in this document	Source	Evidence strength	Limitations
Wharton's Jelly contains one of the highest MSC densities of perinatal tissues	Drobiova et al., Front Cell Dev Biol, 2023. PMID 37440921	High, peer-reviewed review	Review synthesizes prior primary studies
Secretome comprises soluble factors plus extracellular vesicles	Drobiova et al., 2023	High	None noted
Secretome shows immunomodulatory, anti-fibrotic and angiogenic activity	Drobiova et al., 2023	High preclinical, moderate clinical	Predominantly in vitro and animal evidence; human trials limited
Small clinical studies exist in GVHD, diabetes and COVID-19	Drobiova et al., 2023, citing primary trials	Low to moderate	Small trials and case series; not generalizable

References

[1] Drobiova H, Sindhu S, Ahmad R, Haddad D, Al-Mulla F, Al Madhoun A. Wharton's jelly mesenchymal stem cells: a concise review of their secretome and prospective clinical applications. Front Cell Dev Biol. 2023 Jun 27;11:1211217. DOI 10.3389/fcell.2023.1211217. PMID 37440921. PMCID PMC10333601.