

Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

MFGE8

Evidence Summary

Normally has anti-inflammatory effects and can promote recovery from organ damage in the acute phase. Microenvironment influences function, and some conditions can promote pathological processes.

Neuroprotective Benefit: Protective after acute inflammatory brain injury in preclinical models, but could promote loss of stressed but viable neurons in chronic phase.

Aging and related health concerns: May be beneficial as an acute therapy for wound healing and mitigating inflammation-mediated organ damage after injury. High vascular Mfge8 is associated with arterial thickening. Function may be altered in diabetes.

Safety: No evidence of toxicity for recombinant Mfge8 in animal studies, but has not been tested in humans. Treatment likely to have pleiotropic effects and a good benefit/side effect profile may be contingent on localized administration.

Availability: Research use	Dose: Not established	Chemical formula: Protein MW: 387 aa, 43.1 kDa
Half-life: Not disclosed. May vary with formulation.	BBB: Penetrant if associated with exosomes, free recombinant protein unlikely to be penetrant	
Clinical trials: None	Observational studies: None, but 5 studies have examined the associations of serum Mfge8 levels with diabetes and heart disease.	

What is it? Milk fat globule-EGF factor 8 protein (Mfge8), also known as lactadherin, is a secreted glycoprotein [1]. It is a peripheral membrane protein that is associated with extracellular vesicles, and is secreted from cells as an extracellular vesicle-Mfge8 complex [2]. Mfge8 contains aminophospholipid binding sites that bind with phosphatidylserine (PS), which is exposed on the cell membrane of apoptotic cells and serves as an 'eat me' signal. It also contains an RGD domain that allows it to interact with integrins, primarily $\alpha v \beta 3$ and $\alpha v \beta 5$. The presence of these two binding domains allows Mfge8 to act as an opsonin, or molecule that facilitates phagocytic engulfment [3]. Through its interaction with integrins, Mfge8 plays important roles in tissue homeostasis by regulating intracellular signaling events [1]. It is involved in immune regulation, and typically exerts anti-inflammatory activity through inhibition of TLR4 and NF-kb mediated signaling. Consequently, decreased levels of Mfge8 are associated with inflammatory autoimmune diseases [4]. However, the downstream effects of Mfge8-interactions are dependent upon the identity of the specific integrin partner and the associated downstream signaling processes that are triggered by this interaction in a given cell type. Thus, the effects are pleiotropic and context dependent. Mfge8 is also highly expressed in adipose tissue and is important in lipid uptake [5].

Recombinant Mfge8 has primarily been tested in preclinical models of sepsis and acute organ injury where it has been shown to reduce damage and promote recovery.

Neuroprotective Benefit: Protective after acute inflammatory brain injury in preclinical models, but could promote loss of stressed but viable neurons in chronic phase.

Types of evidence:

- 1 study in postmortem brain tissue from AD patients and controls.
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function? None

Human research to suggest benefits to patients with dementia: None

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Alzheimer's disease: Potential mixed benefit (prevention)/harm (established disease) (preclinical)

High levels of Mfge8 may be protective against the onset of Alzheimer's disease (AD) by promoting the clearance of A β by microglia and astrocytes. However, high Mfge8 may exacerbate neuronal loss in the context of ongoing neuronal stress and pathology by inducing apoptosis-mediated cell death (phagoptosis) of stressed, but otherwise viable neurons, that are exposing PS.

In comparing post-mortem brain tissue from AD (n=52) and non-demented controls (n=58), Mfge8 mRNA was decreased by 35% in the AD brain [6]. Mfge8 expression was found to be highest in astrocytes and was enriched in astrocyte-derived exosomes in cell culture [6]. Notably, in the AD brain, Mfge8 was low or absent in areas of high A β load and near amyloid plaques. Similarly, Mfge8 brain expression was also reduced in the Tg2576 AD model compared to age-matched wildtype mice [7].

In cell culture, Mfge8 surrounds A β and can facilitate its phagocytic uptake by glial cells [8]. However, the ability of A β to promote pro-inflammatory processes that reduce Mfge8 secretion may act to inhibit A β uptake *in vivo*, which may explain why AD plaques are devoid of Mfge8. A β promotes microglial production of TNF α and IL-1 through induction of pro-inflammatory NF-kB mediated signaling [9; 10; 11]. Astrocytes exposed to conditioned media from these inflammatory M1-like A β -exposed microglia adopt an inflammatory pathogenic A1-like state, which have reduced secretion of Mfge8 [11]. Mfge8 levels are thought to be a key rate-limiting component in driving phagocytic clearance, therefore reducing Mfge8 availability could be a mechanism to impair A β clearance.

Since Mfge8 has anti-inflammatory properties, the presence of high levels of Mfge8 at the time that an inflammation-inducing stimulus is present could help mitigate or prevent the induction of the



inflammatory response and associated damage. Pre-treatment of the microglia or astrocytes with recombinant Mfge8 prevented the A β -mediated inflammation, and instead promoted adoption of an anti-inflammatory (M2 or A2-like) state by reducing NF- κ B mediated signaling and increasing P13k-Akt mediated signaling [9; 10; 11].

However, Mfge8 is a double-edged sword in AD because it can also facilitate the phagocytosis of viable neurons that have been induced to expose PS in response to environmental stressors, such as inflammatory mediators, oxidative stress, or excitotoxicity [7; 12]. Fractalkine (CX3CL1) is a ligand for the CX3CR1 receptor on microglia that is important for cell migration and phagocytosis. It serves as a 'find me' signal released by neurons following cell stress in order to recruit microglia to apoptotic cells and also stimulates microglial Mfge8 production [7]. Usually, the induction of this system is neuroprotective, but in the presence of AD-associated pathology, particularly aggregated tau, this system may exacerbate neurodegeneration. In tau overexpressing P301S-tau transgenic mice, brain Mfge8 protein expression was found to be elevated [13]. Mfge8 protein levels were also increased in brain regions with high tau from patients with 3 different types of inherited tauopathies [13]. The increase in Mfge8 appeared to be related to tau because elevated levels were not found in brain regions without tau pathology, or in individuals with TDP-43 associated pathology. In cell culture, neurons with tau aggregates had higher reactive oxygen species (ROS) and increased PS exposure, leading to opsonization by Mfge8 and subsequent phagocytic uptake by microglia.

These studies suggest that Mfge8 inducing therapy would only be feasible either as a preventative, or when coupled with another therapy which could prevent stressed viable neurons from exposing PS, such as an antioxidant.

Parkinson's disease: Potential acute stage benefit (rodents)

In an inflammatory rat model of Parkinson's disease (PD), where lipopolysaccharide (LPS) injection into the substantia nigra induces the loss of dopaminergic neurons, the co-administration of recombinant human Mfge8 (rhMfge8) protected against LPS-induced neuronal loss, likely by preventing inflammatory microglial activation [14]. It is unclear whether Mfge8 would also be beneficial after the onset of damage or whether it would contribute to the loss of dopaminergic neurons during the chronic phase.

Stroke/Traumatic brain injury (TBI): Potential mixed benefit (acute)/harm (chronic) (preclinical)

The effects of Mfge8 are context dependent in relation to changes in the brain microenvironment following injury. High levels of Mfge8 may be protective at or near the time of injury to mitigate



damage and clear debris, but may promote neuronal loss in a chronic phase of prolonged stress leading to PS exposure on viable neurons. This time dependency may explain the differential effects of Mfge8 therapeutic interventions in preclinical models.

In the context of cerebral ischemia (MCAO), treatment with rhMfge8 (160 ug/kg) 1-hour post-injury, reduced neurological deficits by 25-30% and infarct size by ~30% 24 and 48 hours later in rats [15]. Mfge8 reduced the production of pro-inflammatory cytokines (TNF α , IL-6) by microglia, neutrophil influx, apoptosis, and necrosis. Some of the anti-inflammatory effects may have been mediated by an increase in PPAR γ (by 39%), which is known to suppress NF-kB activation. In a separate study, intracerebroventricular rhMfge8 immediately following MCAO also reduced neurological deficits and promoted neural stem cell proliferation within 7 days [16]. Treatment with rhMfge8 (intracerebroventricular) 1-hour post-TBI reduced brain edema, neurological deficit scores, and number of apoptotic neurons within 24 hours [17]. The anti-apoptotic effect was driven by P13K-Akt signaling in an integrin-dependent manner. Co-administration of intracerebroventricular recombinant mouse Mfge8 (rmMfge8) with LPS prevented LPS-induced inflammation (TNF α , IL-6) and induction of oxidative stress (decreased ROS, MDA and increased GSH, SOD) in mice [18]. The protective effects appear to be mediated, in part, by preventing the suppression of the Nrf2 endogenous antioxidant pathway.

When moving from the acute to chronic phase, the presence of excess Mfge8 becomes detrimental. Mfge8 was found to be transiently elevated by macrophages/microglia 3-7 days after endothelin-1 induced focal brain ischemia in mice, and led to the phagocytosis of viable PS-exposing neurons in the penumbra, thereby increasing infarct size and neurological deficits [19]. LPS-induced inflammation can also induce an Mfge8-dependent delayed loss of viable neurons [20]. At this later time, eliminating or antagonizing Mfge8 can improve recovery and reduce neurological deficits.

This suggests that recombinant Mfge8 or an Mfge8-inducing therapy may be beneficial in the acute phase to prevent the induction of inflammatory and oxidative mediators, but once these deleterious processes have been induced, an Mfge8 antagonist may be more protective.

APOE4 interactions:

No studies have examined whether Mfge8 expression or function is affected by ApoE status or vice versa, but since both play important roles in cellular lipid uptake and transport, the presence of an interaction, particularly in astrocytes, is feasible.

Aging and related health concerns: May be beneficial as an acute therapy for wound healing and mitigating inflammation-mediated organ damage after injury. High vascular Mfge8 is associated with arterial thickening. Function may be altered in diabetes.

Types of evidence:

- 5 studies on serum Mfge8 levels [Heart disease (n=471); Type 2 diabetes (n=168, n=149, n=105, n=55)]
- Numerous laboratory studies

Wound healing: Potential benefit (preclinical)

Mfge8 promotes wound healing in preclinical models through the reprogramming of macrophages and the promotion of angiogenesis.

The inflammatory/polarization state of a macrophage is highly dependent on its microenvironment. In cell culture, macrophages exposed to Mfge8 containing conditioned media from apoptotic endothelial cells adopt an anti-inflammatory (M2-like) profile [21]. rmMfge8 treatment (30 ug/kg) or the adoptive transfer of ex vivo Mfge8-treated macrophages was shown to promote wound closure in mice [22]. The beneficial effects of rmMfge8 were attributed to the induction of M2-like macrophages, production of bFGF, and promotion of cell migration. Mfge8 is induced under hypoxic conditions and promotes VEGF-dependent angiogenesis in an integrin-dependent manner by promoting Akt phosphorylation [23]. rhMfge8 (subcutaneous) treatment improved post-ischemic neovascularization in mice [23]. Reperfusion after ischemia normally leads to a decline in Mfge8, and treatment with rmMfge8 during reperfusion attenuated the induction of inflammation and oxidative stress, by reducing M1-like macrophage and neutrophil infiltration [24]. Levels of Mfge8 were found to be reduced in the wounds of diabetic patients, and the Mfge8 that was present was in a highly glycosylated form, which has reduced affinity for PS [25]. rmMfge8 also promoted wound healing in diabetic mice (db/db) by promoting anti-inflammatory M2-like macrophages with high phagocytic capacity, and accelerating angiogenesis [25]. Notably, the wound healing capacity of mesenchymal stem cells (MSCs) was found to be dependent on their secretion of Mfge8 in this model.

Sepsis: Potential benefit (rodents)

Mfge8 protects against organ injury in preclinical models of sepsis through its anti-inflammatory and anti-fibrotic activity. Recombinant Mfge8 has been shown to be protective in various preclinical models of sepsis through the reduction of serum levels of organ injury markers and pro-inflammatory cytokines



[26; 27; 28; 29; 30]. Mfge8 significantly improved survival, which was mediated by its ability to protect against intestinal damage and associated weight loss.

Colitis: Recombinant Mfge8 was found to decrease colitis in mouse models by preserving intestinal histological integrity, preventing weight loss, reducing levels of neutrophil chemoattractants and associated neutrophil infiltration, and reducing levels of pro-inflammatory cytokines and apoptotic cells in an integrin-dependent manner [31; 32]. rhMfge8 (166 ug/kg s.c.) treatment was found to improve survival from 31% to 75% ($P < 0.05$) when administered 6 hours after whole body irradiation (7.5-10 Gy) due to the preservation of nutrient absorbing cells in the intestine [33].

Lung injury: Recombinant Mfge8 was found to protect against sepsis-induced or LPS-induced acute lung injury by facilitating the apoptotic cell clearance, and by reducing neutrophil infiltration and pro-inflammatory cytokine production [27; 29; 34].

Renal injury: Recombinant Mfge8 protected against sepsis-induced or ischemic acute renal injury by reducing inflammation, apoptosis, necrosis, and neutrophil infiltration, leading to an improvement in kidney function (decreased BUN and creatine levels) [26; 35; 36]. It also improved capillary function by increasing VEGF expression, and by reducing endothelial-1 and endothelial adhesive molecules (ICAM-1, PECAM-1) [26]. rMfge8 reduced activation of the NLRP3 inflammasome, and mitigated fibrosis (collagen deposition) [36].

Liver injury: Patients with the chronic liver diseases, hepatitis and cirrhosis were found to have decreased hepatocyte expression of Mfge8 [37]. In acute liver injury models, recombinant Mfge8 treatment could reduce hepatocyte loss by inhibiting the pro-apoptotic pathway (via IREa/ASK1/JNK) while also promoting hepatocyte proliferation (through ERK1/2 and Akt) [18; 37; 38]. Mfge8 also reduced the expression of fibrotic factors through inhibition of TGF signaling [37]. Mfge8 was found to be the secreted factor in umbilical cord-derived MSCs responsible for their anti-fibrotic effects in mice [37]. The protective anti-inflammatory effects have been attributed to the modulation of PPAR γ and NF-kB signaling [38].

Cardiovascular: Potential mixed

Age-related aortic remodeling: High levels associated with harm

Mfge8 protein levels were found to increase 2.3-fold in the aortas and arteries of rats during aging (from 8 to 30 months) [39; 40]. Aortic Mfge8 was also found to be increased 9-fold in non-human primates and 6.5-fold in humans during aging, and was primarily in a glycosylated form [39]. Mfge8

promotes vascular smooth muscle cell (VSMC) proliferation in an integrin-dependent manner by triggering ERK1/2 phosphorylation [40]. Angiotensin II promotes expression of Mfge8 by VSMCs, which enhances their invasive capacity [39]. These changes are associated with age-related aortic and arterial wall thickening.

Atherosclerosis: High levels associated with harm, depending on cell type

Preclinical models suggest that the role of Mfge8 in the vasculature is context dependent based on the cell type, microenvironment, and the form of Mfge8. Since the downstream effects of Mfge8 are typically tied to its induction of integrin-dependent signaling, they will vary based on the environmental milieu of integrin receptors and associated interacting proteins. In this way, Mfge8-receptor engagement can have diverse cell-type specific effects.

A cross-sectional study found that serum levels of Mfge8 were higher in healthy older adults ($n=25$, age 67.5 ± 7.5 years) than in healthy young adults ($n=25$, age 24.6 ± 4.0 years), and were highest in diabetic patients (age 70.6 ± 7.3 years) with microvascular complications [41]. Carotid-femoral pulse wave velocity, a measure of arterial stiffness, was associated with Mfge8 levels in diabetic patients, but there was no significant association in healthy individuals, and a separate study found that serum levels were lowest in diabetic patients with vascular complications (age 60.3 ± 9.9 years) compared to those without vascular complications (age 47.4 ± 9.9 years) [42]. Mfge8 serum levels have been positively correlated with LDL-c levels in patients with atherosclerotic disease ($r = 0.182$, $p = 0.026$) [42].

Mfge8-related activity in VSMCs promotes age-related atherosclerotic processes. Increased levels of a glycosylated form are associated with aortic and arterial wall thickening due to effects on VSMCs [39; 40]. Mfge8 is implicated in vascular amyloidosis, since Mfge8 can be cleaved internally to generate a 50 amino acid fragment called medin amyloid, which has been found to be associated with the inflammatory exudate of large arteries [43]. An analysis of postmortem vascular tissue ($n=18$) indicated that arterial medin amyloid levels increased with age, and was most prominent in the aorta [43]. A rat study indicates that increases in VSMC PDGFR- β can activate MMP-2, which in turn leads to increased cleavage of Mfge8 to form medin [44]. Mfge8 containing microparticles are released from endothelial cells that become activated or apoptotic following exposure to advanced glycation end-products (AGEs) [45]. Mfge8-mediated internalization of these particles by surrounding cells can promote the formation of ROS, the induction of inflammatory processes, and influence vascular remodeling.



In contrast, Mfge8 promotes the phagocytotic clearance of apoptotic cells and debris by macrophages, which may be beneficial for reducing plaque burden, as Mfge8 deficiency in mice can accelerate atherosclerosis.

Heart disease: High levels may be protective

Several studies have found an inverse association between Mfge8 levels and measures of heart disease or dysfunction. Patients with coronary atherosclerotic heart disease (n=176) were found to have lower levels of serum Mfge8 than age-matched healthy controls (n=295) (673.20 ± 112.34 ng/mL vs. 134.89 ± 4.74 ng/mL, $p < 0.001$) [46]. Patients with heart disease also had more unfavorable lipid profiles (higher TG, LDL-c, LDL-c/HDL-c). Furthermore, the serum Mfge8 levels decreased with disease severity (inverse correlation with the Gensini score, $r = -0.590$, $p < 0.001$). The effect was largely driven by a negative association between Mfge8 and the inflammatory marker high sensitivity-CRP ($r = -0.105$, $p = 0.022$). Similarly, an inverse correlation was found with the severity of cardiac dysfunction (LVEDd) and circulating Mfge8 levels in patients with cardiomyopathy (n=162) ($r = -0.3550$, $p < 0.0001$) [47].

Mfge8 knockout mice have higher levels of cardiac pathology and fibrosis after aortic banding surgery due to potentiation of Akt/GSK3 β /mTOR signaling. Pre and post-treatment with rhMfge8 (150 ug/kg i.p.) prevented activation of this pathway and reduced the level of surgery-associated cardiac hypertrophy. rmMfge8 administered intramyocardially immediately after surgery promoted apoptotic cell clearance in the infarct area, reduced inflammation, and improved survival in a mouse model of myocardial infarction [48]. These studies suggest that treatment with Mfge8 prior to cardiac surgery or administered closely after the onset of heart damage could facilitate recovery and mitigate damage.

Diabetes: Mfge8 is dysregulated and may promote harm in this context

Mfge8 may be dysregulated in the context of diabetes since diabetics have been shown to have higher levels of glycated Mfge8, which has lower binding affinity for PS, and Mfge8 dysregulation may be a downstream effect of altered glucose/insulin levels.

Patients with Type 2 diabetes have been shown to have increased serum levels of Mfge8, which may stem from ability of insulin to induce Mfge8. Two studies have also found that elevated Mfge8 levels were correlated with increased arterial stiffness, as assessed by pulse wave velocity [(n=105; $r = 0.360$, $p < 0.01$) (n=55; $r = 0.481$, $p < 0.01$)] [41; 49]. However, there are conflicting studies with regards to the association between Mfge8 levels and vascular complications in diabetic patients [42]. In a diabetic mouse model (db/db), elevated Mfge8 was associated with increased aortic remodeling, VSMC

proliferation, endothelial inflammation, and renal injury [49; 50]. These effects were exacerbated by administration of recombinant Mfge8, and driven by ERK1/2 activation and associated signaling.

Notably, serum levels of Mfge8 were modified by body weight, as obese individuals had lower mean serum levels than lean individuals [157.82 95% CI (140.12 to 187.80) vs 211.46 95% CI (167.58 to 293.01 pg/mL); $p < 0.001$] [18]. The lower circulating levels of Mfge8 were also associated with higher levels of systemic inflammation (TNF α). Mfge8 is very highly expressed in adipocytes, and is increased in the adipose tissue from obese people [51]. It plays a critical role in fatty acid uptake and release through modulation of surface expression of the fatty acid transporter CD36 [5]. Mfge8 has also been shown to be important for nutrient absorption in the intestine in preclinical models [52; 53]. Since fatty acids can induce inflammatory toxicity, increased fatty acid uptake and sequestration into lipid droplets is cytoprotective, and may explain some of the benefits of Mfge8 in the context of colitis. However, it also influences triglyceride release by regulating lipid droplet hydrolysis [52]. These lipid modulating effects utilize the same P13K/Akt signaling machinery used by insulin, thus excessive Mfge8-mediated fat absorption could potentially contribute to insulin resistance. That lower levels of serum Mfge8 are associated with higher levels of triglycerides in diabetic patients [42] could occur because more Mfge8 is needed to facilitate lipid uptake into cells, and thus is being taken out of circulation. It is not known whether organ levels of Mfge8 are altered in diabetic patients in a way that could account for the change in circulating levels.

These studies suggest that the changes in the body which occur in diabetic patients, such as high glucose levels, may negatively impact the function of Mfge8, such that it promotes pathogenic processes rather than ameliorative ones.

Cancer: High levels associated with worse prognosis

High levels of Mfge8 are associated with worse prognosis in the context of various cancers. In colorectal cancer tissue Mfge8 expression was higher in later stages than early stages, and high Mfge8 was associated with metastasis [54]. *In vitro*, Mfge8 knockdown can suppress tumor cell growth and invasion, which is partially dependent on P13K/Akt signaling. Mfge8 can also impair tumor immunosurveillance by promoting the polarization of M2-like tumor infiltrating macrophages and by promoting neovascularization [23; 55].

Safety: No evidence of toxicity for recombinant Mfge8 in animal studies, but has not been tested in humans. Treatment likely to have pleiotropic effects and a good benefit/side effect profile may be contingent on localized administration.

Types of evidence:

- Numerous laboratory studies

Recombinant Mfge8 therapies have not been tested in humans. While Mfge8 is safe as an endogenous protein, recombinant Mfge8 is not processed in the same way as *in vivo*, and thus may not have the same biological properties. However, there is no evidence of toxicity in preclinical models and the recombinant protein was generally found to mimic the activities of the endogenous protein in these studies [28; 31]. Mfge8 treatment alone tended to not exert any overt effects, and its actions were only observed in the context of some type of stimulus such as inflammation or organ damage. Since Mfge8's effects are highly context dependent, its use as a therapy would need to be administered in a localized and/or time dependent manner. Systemic administration of Mfge8 is likely to have pleiotropic effects, and chronic use may exacerbate vascular remodeling [40]. Exogenous Mfge8 has only been used as an acute treatment in animal models, thus potential side effects of long-term use are not known.

Sources and dosing:

Recombinant human Mfge8 is available from commercial suppliers for research use ([R&D Systems](#)), but is not currently available as a therapeutic agent for clinical use.

MSCs: Several preclinical studies have indicated that Mfge8 is part of the MSC secretome, and may be involved in some of the angiogenic, anti-inflammatory, and anti-fibrotic effects of MSC therapy [25; 37].

Mfge8 modulating therapies: High tissue levels of Mfge8 have been shown to be associated with disease worsening in the context of arterial disease, such as atherosclerosis, and in diabetes. Several effective anti-hypertensives, such as ACE inhibitors and beta blockers are known to decrease levels of vascular Mfge8. Polyphenol polymers also reduce vascular expression of Mfge8. Anti-diabetic drugs may also alter Mfge8 levels by modulating insulin and glucose levels [4].

Research underway:

There are no clinical trials currently underway testing the use of Mfge8 as a therapeutic agent.

[Therasource LLC](#), has been trying to develop recombinant human Mfge8 for therapeutic use for acute kidney disease, hemorrhagic shock, and inflammatory bowel disease based on promising preclinical data in these areas. The company was founded by Dr. Ping Wang of the Feinstein Institute for Medical Research, whose lab has published many of the preclinical studies in this area. The company has



received SBIRs for rhMfge8 in 2013 and 2016, but there have been no updates about progress from the company since 2017, and it is unclear whether development is still ongoing.

Dr. Jean-Francois [Cailhier](#) at the University of Montreal is working on developing a dermatologic wound healing therapy for diabetes and burns. The treatment is an autologous cell therapy where macrophages are reprogrammed *ex vivo* with Mfge8 to induce an anti-inflammatory phenotype. They have established proof-of-principle in preclinical models, but this therapy has not yet been tested in a clinical population.

Exosome mediated therapies:

Mfge8 is localized to exosomes as a peripheral membrane protein through its C1C2 domain [2]. Extracellular vesicles can be engineered to display soluble antigens or the extracellular domains of membrane proteins of interest by fusing them to the C1C2 domain [56]. Some groups have been using this technology to optimize antigenicity of cancer vaccines by using the domain to target tumor associated antigens to exosomes [57]. The exosomes could then directly transfer these antigens to antigen presenting cells.

Search terms:

Pubmed, Google: Mfge8 or lactadherin +

Alzheimer's disease, Parkinson's disease, stroke, neurodegeneration, phagocytosis, aging, atherosclerosis, cardiovascular, cancer, diabetes, inflammation, recombinant therapy, wound healing, safety

Websites visited for Mfge8:

- [PubChem](#)

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