



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.

Plasma Exchange

Evidence Summary

Some evidence suggests that plasma exchange or plasma infusions may be beneficial for Alzheimer's and other age-related diseases, though the optimal formulation is unknown.

Neuroprotective Benefit: Preliminary evidence suggests that plasma may be beneficial in AD patients, though the best type of plasma fraction is still unknown.

Aging and related health concerns: Multiple preclinical studies suggest that treatment with plasma (or plasma dilution) can increase lifespan and improve multiple age-related pathologies.

Safety: Most side effects are mild and rare serious adverse events can usually be managed and may be due to certain components in the plasma product (e.g., IVIG).



<p>Availability: Grifols' and Alkahest's proprietary plasma exchange is not currently available, though traditional plasma exchange is available for certain indications.</p>	<p>Dose: Grifols: during the six-week intensive treatment, 2500-3000 mL of plasma is replaced along with 5% albumin; during the long-term phase, 650-880 mL of plasma is removed and replaced with an addition of 80-200 mL of 5% albumin with or without 10-20 g of IVIG. Alkahest: Typically, patients are treated with 250 mL of Alkahest's proprietary plasma fraction.</p>	<p>Molecular formula: N/A Molecular weight: N/A</p>
<p>Half-life: N/A</p>	<p>BBB: Some components of the plasma are probably penetrant</p>	
<p>Clinical trials: Grifols: two clinical trials with a total of 389 patients in AD. Alkahest: Three trials with a total of 82 patients in AD and one trial with 89 patients in PD.</p>	<p>Observational studies: None</p>	

What is it?

The first study showing that parabiosis could increase lifespan was conducted in 1972 by [Ludwig and Elashoff](#). The circulatory systems of young and aged rats were connected (heterochronic parabiosis), and the aged rats lived ~100 days longer than aged rats connected to other aged rats (homochronic parabiosis). Since then, several other lines of research have been pursued to increase lifespan and healthspan: infusion of young plasma, dilution of aged plasma with saline, and identification of factors in young blood.

Therapeutic plasma exchange (PE) is the process of removing plasma from an individual via plasmapheresis (centrifuging the blood to remove just the plasma and returning the rest of the blood to the patient) and replacing it with donor plasma. Plasma exchange is used for several neurological



disorders including Guillain-Barre syndrome, multiple sclerosis, inflammatory demyelinating polyradiculoneuropathy, acute inflammatory demyelinating disease of the CNS and other peripheral neurological conditions ([Imbimbo et al, 2020](#)).

Grifols is the first company to try this approach in Alzheimer's disease. They conducted PE with albumin in AD patients. However, their initial hypothesis was not that young factors may improve cognition. Rather, they suggested that treatment with albumin itself may reduce amyloid in the brain. Amyloid in the cerebral spinal fluid (CSF) is in dynamic equilibrium with amyloid in the plasma. The "sink hypothesis" is that if you remove peripheral amyloid, then more amyloid will leave the brain and enter the plasma. In the blood, amyloid is sequestered in albumin, therefore, by replacing plasma in AD patients with plasma supplemented with albumin, it may reduce brain amyloid levels ([Boada et al, 2020](#)).

In AD patients, albumin is more glycosylated and nitrotyrosinated than albumin from healthy subjects which can reduce its ability to sequester blood amyloid and to reduce amyloid aggregation ([Loeffler, 2020](#)). In addition, oxidation of a free thiol (Cys-34 residue) and carbonyl formation on the Pro, Arg, Lys, and Thr residues on albumin is thought to be linked to aging ([Tang et al, 2021](#)).

An alternative hypothesis is that plasma infusions may remove detrimental plasma factors in elderly individuals or may introduce young systemic factors that are beneficial. [Kheifets and Braithwaite \(2019\)](#) named these factors "chronokines".

Neuroprotective benefit: Preliminary evidence suggests that plasma may be beneficial in AD patients, though the best type of plasma fraction is still unknown.

Types of evidence:

- Two RCTs with Grifols plasma product
- One dose-finding study with GRF6019 in mild-to-moderate AD patients
- One RCT with GRF6019 in severe AD patients
- One RCT with GRF6019 in patients with Parkinson's disease
- One cross-over trial with young fresh frozen plasma in patients with AD
- Multiple preclinical studies in animals treated with plasma, young factors, or subjected to parabiosis



Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

None

Human research to suggest benefits to patients with dementia:

Grifols Therapeutic Plasma Exchange

347 patients with Alzheimer's disease were randomized to either sham treatment or plasma exchange (PE). For the first six weeks, the active group received weekly treatments with "high-volume" PE (2,500-3,000 mL of plasma with 5% Albutein). During this period, a peripheral or central venous catheter was placed in the subclavian or jugular vein. This was followed by 12 months of monthly "low-volume" PE (650-800 mL) in the following four groups: sham treatment, PE with 20g of albumin (5% Albutein) (low-albumin group), PE with 20 g of albumin alternated with 10 g IVIG (Flebogamma 5% DIF) (low-albumin+IVIG group), or PE with 40 g of albumin alternated with infusions of 20 g IVIG (high-albumin+IVIG group). During the "low-volume" period, plasmapheresis was performed via a peripheral vein ([Loeffler, 2020](#)).

For the placebo arm, during the "high-volume" PE, a sham central catheter was placed on the skin which did not actually puncture the skin. During the "low-volume" PE, a needle was inserted into the arm and a sham centrifugation was performed, but no new plasma was put into the patient.

After 14 months, there was less decline on the ADCS-ADL (a measure of function) for patients in the combined PE groups with no difference between the treatment arms. However, this difference was only significant for patients with moderate AD but not mild AD. There was also a trend for improvement on the ADAS-Cog (a measure of cognition) which was significant for the moderate AD group but not for the mild AD group. Again, there were no differences across the different treatment arms. On the CDR-sb (a global measure of cognition and function, and a common outcome measure for phase 3 trials), the combined treatment arms improved compared to the placebo group for both mild and moderate AD patients (and, in fact, the mild patients improved from baseline).

In a biomarker sub-study (n = 297), CSF levels of A β 42, tau, and p-tau levels improved in the moderate patients after the 6-week run-in period. However, tau and p-tau increased in the mild group at the end of the 12-month treatment period ([Boada et al, 2020](#)).



In another study, patients underwent PE with 5% albumin (Albutein) over three treatment periods: 1) intensive treatment: 3 weeks with two PE per week; 2) maintenance treatment period I: 6 weekly PE treatments; 3) maintenance treatment period II: 12 weeks of bi-weekly treatments. Patients were followed for 6 months. No difference was reported in hippocampal volume, posterior cingulate, or total intracranial volume between the treatment or control group. However, a greater percentage of patients in the treatment group had improvement in cerebral perfusion while a greater percentage of control patients showed worsening cerebral perfusion ([Gemma Cuberas-Borros et al, 2018](#)).

Another analysis from the same study suggested that there was a trend for increased CSF A β 42 and a drop in plasma A β 42. Plasma levels of A β 42 and 40 levels presented in a “saw-tooth” pattern, where levels dropped after each treatment period and increased before the next treatment (suggesting that the treatment reduced plasma amyloid levels). There were no significant differences on any cognitive or functional measure (global cognition, language/attention tests, behavioral/functional tests), although there were trends of improvement which could be clinically relevant. In the treatment arm, patients scored worse on the neuropsychiatric inventory (NPI). Adverse events were balanced between the two groups, and most were related to the study procedure rather than the plasma itself ([Boada et al, 2017](#)).

One caveat for the previous two studies is that for the intensive treatment periods (6 weeks for AMBAR, 3 weeks for the phase 2), a central catheter is inserted in treated patients and left there for the treatment period while control patients are given a “sham” catheter. After the intensive treatment periods, treated and control patients have peripheral venous catheters inserted. Most of the adverse events happened during these intensive treatment periods and [Boada et al \(2017\)](#) suggested that the worsening scores on the NPI may be due to anxiety in patients having this central catheter during the intensive treatment period. Future studies will have to examine whether this intensive treatment period is necessary.

Alkahest Plasma Therapy

In the following Alkahest studies, plasmapheresis is not done so plasma is not exchanged, rather young fractions of plasma are infused. There are some safety concerns with the use of therapeutic plasma exchange including the risk of the transfer of pathogens, histo-incompatibility, and allergic reactions to proteins like clotting factors and immunoglobulins. Therefore, Alkahest pools plasma from multiple donors, and the plasma fraction is depleted of coagulation factors and gamma globulins. GRF6019 contains approximately 400 proteins that are thought to mediate the beneficial effects of plasma from young donors. In preclinical studies, GRF6019 increased neurogenesis, improved learning and memory,



and reduced inflammation. It was also reported that pulsed dosing (5-7 daily infusions) in rodents was superior to intermittent dosing (2-3 doses per week) ([Imbimbo et al, 2020](#)).

In a cross-over trial, nine AD patients were randomized to be treated with 250 mL of young fresh frozen plasma (not GRF6019 but pooled from donors ages 18-30) or placebo over four weekly infusions with a six-week washout period in between. There were no changes in cognition or psychiatric assessments (ADAS-Cog13, CDR-SB, and NPI), though plasma treatment improved functional scores (Functional Activities Questionnaire and ADCS-ADL). There were no changes in functional connectivity in the brain (resting-state fMRI) ([Sha et al, 2019](#)).

A study of GRF6019 in 47 mild-to-moderate AD patients reported no differences in adverse effects between a 100 mL and 250 mL dose over 24 weeks. Patients were treated for five consecutive days at weeks 1 and 13. The infusions took two hours to complete. Although not statistically powered to show difference between the two groups, cognitive scores were numerically better in the 250 mL group ([Hannestad et al, 2020](#)). There was another study in 26 severe AD patients treated with GRF6019 (250mL) or placebo for five daily infusions with a four-week follow-up period. There were no differences in cognition or adverse events between the two groups ([Hannestad et al, 2021](#)).

In a phase 2 study in 89 patients with Parkinson's-dementia, treatment with GRF6021 (250ml for five days at day 1 and 85) over six months improved executive function, verbal abstraction, and orientation (presented at AD/PD conference, 2021).

Mechanisms of action for neuroprotection identified from laboratory and clinical research

[Kim et al \(2020\)](#) collected plasma from young mice that had exercised for three months. They infused 100 μ L (intravenously, i.v.) of this plasma into 12-month-old AD mice (3xTg-AD) 10 times at 3-day intervals and compared this to injection of plasma from young mice that did not exercise. Mice infused with plasma from young mice that had exercised had higher levels of plasma BDNF, improved memory, improved mitochondrial function, less cell death in the hippocampus, and higher levels of synaptic proteins. There were no differences in p-tau levels. For most outcome measures, mice infused with plasma from young mice that had not exercised were not significantly different than control AD mice with no plasma infusions.

[Villeda et al \(2014\)](#) reported that heterochronic parabiosis increased the expression of genes involved with synaptic plasticity in the hippocampus of aged mice and increased the protein expression of immediate early genes (e.g., Egr1, c-Fos – proteins involved with synaptic activity). In addition,



heterochronic parabiosis increased dendritic spine number in the dentate gyrus and long-term potentiation (LTP) but had no effect on synaptic strength. Treatment of aged mice with plasma from 3-month-old mice (100 μ L eight times over 24 days, i.v.) also improved contextual fear memory and learning and memory on the radial arm water maze test compared to treatment with plasma from old mice. These effects were abrogated when aged mice were treated with heat denatured young plasma. [Villeda et al \(2011\)](#) also reported that CCL11 (eotaxin) increases in the human CSF and plasma with age and that administration of CCL11 to young mice impaired neurogenesis and learning and memory (fear memory and radial arm water maze test).

[Middeldorp et al \(2016\)](#) reported that five-week heterochronic parabiosis in AD mice (APP, young mice were 2-3 months, old mice 16-20 months) increased synaptic (synaptophysin) and neuronal (calbindin) proteins but had no effect on amyloid or microglia. Infusion with young plasma (150 μ L, twice per week for four weeks, i.v.) also increased synaptic and neuronal proteins and improved working and contextual (but not cued) fear memory.

Aged immunodeficient (NOD/SCID – NSG) mice were treated with neonatal umbilical cord plasma (175 μ L, i.v.) every two days for two weeks. Treatment increased gene expression of proteins involved with LTP in the hippocampus. A smaller subset of LTP genes was increased when mice were treated with young adult, but not elderly plasma. Changes in LTP gene expression was only seen in the hippocampus and not in the motor cortex or amygdala. There were no changes in neurogenesis. Umbilical cord plasma also increased LTP and improved memory (Barnes maze and contextual fear conditioning). They identified TIMP2 as a potential protein that mediates these beneficial effects, and injection of aged wild type mice with TIMP2 (50 μ g/kg, i.p.) every other day for one week improved LTP and learning and memory performance. In addition, systemic treatment of young mice treated with TIMP-2-depleted umbilical cord plasma had no effect on memory, and treatment of young mice with a TIMP2 neutralizing antibody reduced performance on a spatial memory task suggesting that TIMP2 may mediate some of the beneficial cognitive effects of young plasma ([Castellano et al, 2017](#)).

[Khrimian et al \(2017\)](#) reported that infusion of 16-month-old mice with 3-month-old plasma (100 μ L, i.v.) eight times over 24 days improved memory on a novel object recognition task and reduced anxiety on an elevated plus maze task. However, there were no memory improvements when old mice were infused with plasma from osteocalcin knockout (Ocn $^{-/-}$) mice. In addition, memory was impaired when young mice were treated with an osteocalcin neutralizing antibody, and memory was improved when old mice were treated with osteocalcin over two months.



[Tang et al \(2021\)](#) (preprint) treated middle-aged mice (12-months old) with young and undamaged recombinant serum albumin (rMSA, 1.5 mg/g dissolved in saline, i.v.) every three weeks. rMSA treatment improved learning and memory (on the Barnes Maze test) in male mice (females not tested) and reduced levels of p-tau in male (but not female) mice.

[Mehdipour et al, \(2020\)](#) conducted a study where they replaced half of the plasma in an animal with saline containing 5% albumin (they call it “neutral” blood exchange, NBE – the albumin is to replace the albumin lost in the plasma dilution). NBE treatment in old mice improved hippocampal neurogenesis compared to old mice that had undergone heterochronic blood exchange, and neurogenesis was no longer significantly different than NBE-treated young mice.

They also found that NBE-treated old mice had improved cognition one week after treatment (novel object recognition), reduced neuroinflammation, and fewer senescent cells in the brain. Interestingly, although treatment with navitoclax also reduced senescent cells in the brain (similar to NBE), it did not increase neurogenesis. Navitoclax does not cross the blood brain barrier. This suggests that although removal of SASP factors peripherally may reduce senescence in the brain, it may not be sufficient to restore neurogenesis ([Mehdipour et al, 2021](#)).

[Katsimpardi et al \(2014\)](#) conducted a five-week heterochronic parabiosis experiment in wild type mice. Parabiosis of 2-month-old mice with 15-month-old mice increased neurogenesis in older mice but had no effect in young mice. However, parabiosis of 2-month-old mice with 21-month-old mice impaired neurogenesis in young mice. Heterochronic parabiosis also increased blood vessel volume in old mice by 87% and restored cerebral blood flow to levels seen in young mice. Administration of GDF11 to old (21- to 23-month old) mice partially recapitulated some of the results seen with parabiosis.

APOE4 Interactions:

None reported

Aging and related health concerns: Multiple preclinical studies suggest that treatment with plasma (or plasma dilution) can increase lifespan and improve multiple age-related pathologies.

Types of evidence:

- Six preclinical studies of parabiosis, plasma dilution, extracellular vesicles, or young plasma looking at lifespan and multiple age-related pathologies



[Mehdipour et al, \(2020\)](#) conducted a study where they replaced half of the plasma in an animal with saline containing 5% albumin (“neutral” blood exchange, NBE – the albumin is to replace the albumin lost in the plasma exchange). A single NBE procedure improved muscle regenerative capacity and fibrosis in old mice to the point it was not significantly different from NBE-treated young mice. NBE also reduced liver adiposity and fibrosis after six days. In addition, the investigators took plasma from elderly individuals before and after they underwent therapeutic PE. *In vitro*, plasma from elderly individuals after PE improved myogenic cell proliferation compared to plasma from before PE.

In aged rats, infusion of 1 mL of plasma from young rats (i.v.) three times per week over 28 days reduced markers of oxidative stress (reactive oxygen species, ROS; increased GSH, and reduced lipid peroxidation, MDA). It had no effect on plasma inflammatory markers (TNF α , IL-6) ([Tripathi et al, 2021](#)).

[Yoshida et al \(2019\)](#) reported that plasma levels of eNAMPT (an enzyme that is the rate-limited step for NAD⁺ synthesis) declines with age by 33% (females) to 74% (males) in mice. Plasma eNAMPT was located in extracellular vesicles (EVs) and treatment of aged female mice once per week (i.p) with purified extracellular vesicles isolated from 500 μ L of plasma from young-to-middle aged mice increased mean lifespan by 10.2% and maximum lifespan by 15.8%. Treatment for four days also increased exercise performance in aged mice. These results required eNAMPT, as treatment with extracellular vesicles purified from cultured eNAMPT deficient adipocytes had no effect on exercise performance.

[Tang et al \(2021\)](#) (preprint) treated middle-aged WT mice (12-months old) with young and undamaged recombinant serum albumin (rMSA, 1.5mg/g dissolved in saline, i.v.) every three weeks. rMSA treatment increased lifespan (17.6%, females; 20.3% males) and improved the appearance of the fur (it was glossier and thicker). There were no changes in the amount of fibrosis in the kidney, liver, or heart. Treatment also improved grip strength in both sexes and muscle size in female (but not male) mice. They propose that four modifications to albumin contribute to the aging process – a decrease in free thiols, an increase in carbonyls due to oxidative damage, advanced glycation end products (AGE), and an increase in homocysteine (Hcy).

[Ghosh et al \(2019\)](#) reported that parabiosis between old and young mice over 4 weeks reduced inflammation (e.g., MCP-1, IL-6, CRP) and senescence markers (e.g., p16, p21) in adipose tissue of old mice. *In vitro*, administration of young plasma to aged adipose explants also reduced markers of senescence (p16 and p21) and some markers of inflammation (TNF α and MCP1 but not IL-6).

[Rebo et al \(2016\)](#) created a heterochronic blood exchange paradigm in small animals that did not require connecting the circulatory systems of the animals. Anesthetized mice had a catheter inserted into their jugular vein and 150 μ L of blood were exchanged between animals 15 times with a 30 second delay between transfers. This allowed the homogenization of blood between the two animals. After a single procedure, old animals that had received young blood had an improved regenerative capacity and less fibrosis in muscles. There were no differences in young animals that had received old blood. Opposite results were reported with neurogenesis. Old animals that received young blood had no change in neurogenesis while young animals that received old blood had a reduction in neurogenesis. This suggests that different tissues may respond differently to young or old factors.

Safety: Most side effects are mild and rare serious adverse events can usually be managed and may be due to certain components in the plasma product (e.g., IVIG).

Types of evidence:

- One review on therapeutic plasma exchange
- Two RCTs with Grifols' plasma exchange
- Two RCTs with Alkahest's GRF6019
- One cross-over trial with Alkahest's young fresh frozen plasma

Grifols plasma exchange

347 patients with Alzheimer's disease were randomized to either placebo or plasma exchange (PE). For the first six weeks, the active group received weekly treatments with "high-volume" PE (2,500-3,000 mL of plasma with 5% Albutein). During this period, a peripheral or central venous catheter was placed in the subclavian or jugular vein. This was followed by monthly "low-volume" PE (650-800 mL) in the following four groups: sham PE, PE with 20g of albumin (5% Albutein) (low-albumin group), PE with 20 g of albumin alternated with 10 g IVIG (Flebogamma 5% DIF) (low-albumin+IVIG group), or PE with 40 g of albumin alternated with infusions of 20 g IVIG (high-albumin+IVIG group). During the "low-volume" period, plasmapheresis was performed via a peripheral vein.

During the "high-volume" treatment period, 20.1% of PEs were associated with an adverse event (AE) compared with 13.1% during the "low-volume" period. Product-related adverse events (AEs) were more common in the high albumin+IVIG group (17.7% of patients) compared with the low albumin groups (~7% of patients). The median duration of AEs was one day, with 60% of them being transient (<7 days). Serious AEs (SAEs) were more common in the groups receiving IVIG (1.9% of the PEs performed and 20%



of patients vs. 0.9% of the PEs performed and 10% of patients in the sham group). Most of the SAEs were related to gastrointestinal, metabolic, and neurological symptoms or infections. About 6%-11% of patients in the IVIG groups dropped out (compared to 1.3% in the placebo and low-albumin groups).

The most common AEs in the treatment groups included blood and lymphatic system disorders (25.5% vs. 10.1% of patients in the placebo), anemia (20.6% vs. 6.3%), gastrointestinal disorders (22.6% vs. 12.7%), administration site AEs (36.6% vs. 16.5%), musculoskeletal and connective tissue disorders (25.1% vs. 7.6%), nervous system disorders (41.2% vs. 24.1%), and hypotension (21.8% vs. 1.3%). Many of these AEs were thought to be related to the procedure itself rather than the product specifically ([Boada et al, 2020](#)).

In another study from Grifols, 42 patients underwent PE with 5% albumin over six months (twice per week for three weeks, once per week for six weeks, and once bi-weekly for 12 weeks). Treated patients scored worse on the NPI (a neuropsychiatric test). The most common AEs were infections (due to the infusions; 56% in the treatment arm vs. 29% in the sham arm) and psychiatric disorders (mostly anxiety, 50% vs. 36%). The investigators hypothesized that the psychiatric disorders and worse scores on the NPI could be due to the fact that the treated patient had to live with a catheter inserted in their chest for the initial treatment period ([Boada et al, 2017](#)).

Alkahest plasma treatment

In a cross-over trial with nine patients using fresh frozen plasma (250 mL, from Alkahest) or placebo, there were no differences in adverse events between the groups ([Sha et al, 2019](#)). In a study comparing 100 mL or 250 mL of Alkahest's GRF6019 (five treatments at weeks 1 and 13) in 47 patients with mild-to-moderate AD over 24 weeks, three patients withdrew from the study due to AEs. There were no significant differences in AEs between the two group (87% in the 250 mL, 75% in the 100 mL group). The most common AEs were headaches, diarrhea, falls, arthralgia, transient changes in blood pressure, transient laboratory abnormalities, and infusion-site bruising. Most of the AEs were mild in intensity ([Hannestad et al, 2020](#)). A similar study in 26 severe AD patients treated with GRF6019 (250mL) reported a similar number of AEs between placebo and treatment arms ([Hannestad et al, 2021](#)).

In general, PE is relatively safe with most side effects being mild. The risk of life-threatening adverse events (death, hypotension-requiring a vasopressor agent, arrhythmias, and hemolysis) ranges between 0.025-4.75%. Though most of these can be managed and most occur in individuals with severe pre-existing conditions ([Filipov et al, 2018](#)).



Drug interactions:

Contraindications for PE include allergy to albumin or fresh frozen plasma and individuals who have active sepsis or are hemodynamically unstable ([Filipov et al, 2018](#)).

Sources and dosing:

Therapeutic plasma exchange is available in clinics for certain indications. However, the proprietary formulations for Grifols' and Alkahest's PE are not currently available.

Grifols: during the six-week intensive treatment, 2500-3000 mL of plasma is replaced along with 5% albumin; during the long-term phase, 650-880 mL of plasma is removed and replaced with 80-200 mL of 5% albumin with or without 10-20 g of IVIG.

Alkahest: Typically, patients are treated with 250 mL of Alkahest's proprietary plasma fraction.

Research underway:

There are 100 studies on clinicaltrials.gov for therapeutic plasma exchange. Most of the studies are for Covid-19, liver or kidney failure, or organ transplants.

One study is comparing the effect of plasmapheresis and infusions of plasma from young ApoE3 patients into ApoE4 patients over 12 months. Three patients will have monthly sessions of plasmapheresis over six months, three will have biweekly plasma infusions over six months, and three will serve as a control group. This is primarily a safety study, though exploratory biomarkers (not defined) will be examined as well ([NCT03887741](#)).

Another study is testing the effect of PE with or without albumin in 80 middle-aged participants on aging biomarkers (e.g., traditional blood markers such as blood count, lipids, etc.; the PhenoAge methylation clock; ECG results; etc.). Individuals will get two sessions per week over one month ([NCT04897113](#)).

Preclinical studies are also ongoing including:

- Testing a novel small animal heterochronic blood exchange system that does not require suturing two animals together ([Conboy](#) – see Rebo et al, 2016 in aging section).
- Testing the effect of plasma from aged mice on senescent cell accumulation in young mice ([Schafer](#)).

Search terms:

plasma pheresis + alzheimer, aging, lifespan, apoe4



Conboy + plasma

GRF6019

parabiosis + lifespan

therapeutic plasma exchange + safety [review]

plasma exchange + apoe4

Websites visited:

- Pubmed
- Clinicaltrials.gov
- NIH Reporter

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