Table 1: Summary of hAdMSC treatments of 10 patients with different autoimmune-associated diseases. Detailed clinical case reports are provided in the supplementary information. Multiple sclerosis: *EDSS is expanded disability status scale. Atopic dermatitis: The outcome was evaluated by the area of skin lesions, **SCORAD (SCORing Atopic Dermatitis) index [112,113] and CBC count. The changes of SCORAD index of each patient before and after AdMSCs treatment are summarized in table 1. Rheumatoid arthritis: ***VAS (Visual Analogue Scale) KWOMAC (Korean Western Ontario McMaster). Further information on patient profile and treatment for AIED are summarized in supplementary figure 1.

Case	Age/Sex	Injections and cell numbers	Total cell number received	Clinical status at presentation	Clinical status after treatment	Observation time (months)
Autoimmune inner ear disease (AIED) AIED [93,94] is a progressive, bilateral yet asymmetric, sensorineural hearing loss. Patients have higher frequencies of interferon (IFN)-c-producing T cells and higher serum antibody titres compared with healthy controls and patients with noise- and/or age-related hearing loss [95]. The mainstay treatment for AIED are anti-inflammatory drugs, particularly corticosteroids [96,97]. However, some patients are refractory to steroid treatment. Thus, alternative treatment is needed for these patients. Efficacy of hAdMSCs on experimental autoimmune hearing loss (EAHL) was shown in mice [98]. Mice were immunized with β-tubulin to develop EAHL and treated with i.v. injection of hAdMSCs (once a week for 6 consecutive weeks) resulting in improved hearing, hair cell stabilization, reduced proliferation of antigen-specific Th1/Th17 cells and induced anti-inflammatory cytokine IL-10 in splenocytes, induction of antigen-specific CD4(+) CD25(+) Foxp3(+) regulatory T-cells with the capacity to suppress autoantigen-specific cytotoxic T-cell responses.						
1	19/F	3x each $2x10^8$ (i.v.)	$6x10^8$	Severe progressing hearing loss for 3 years (no in left ear, severe in right ear)	Normal hearing in right ear, moderate hearing in left ear	11
Multiple Sclerosis (MS) MS is a multifocal inflammatory disease of the central nervous system, which mainly affects young women between ages twenty and forty years and causes paralysis of the limbs, sensation, visual and sphincter problems. The disease is clinically evident with relapses of neurological disability due to damage of myelin occurs (plaques of sclerosis). The disease enters a progressive phase due to damage of the axons and irreversible neurodegeneration. Existing immunotherapies downregulate the autoimmune anti-myelin reactivity and reduced the rate of relapses (e.g. INF-β, glatiramer acetate and mitoxantrone) but progression of disability and myelin regeneration is not possible [99,100]. In the chronic EAE animal model [101], BMMSCs and AdMSCs were shown to restore neuronal activity and produce new neurons [102,103]. We demonstrated previously that hAdMSCs ameliorates the symptoms in EAE in a dose- and time-dependent manner, and these effects can be mediated in part by the production of anti-inflammatory cytokines [104].						
2	46/F	5x each $1x10^8$ (i.v.) 3x each $1x10^7$ (intrathecal)	$1.03x10^9$	EDSS* 8	EDSS 7	4
Polymyositis PM is a type of chronic inflammatory myopathy with unknown etiology associated with invasion of white blood cells in muscle tissue. PM is related to dermatomyositis and inclusion body myositis. Clinical signs include pain with proximal muscle weakness and loss of muscle mass, particularly in the shoulder and pelvic girdle. Despite the uncertainty in the exact cause of PM, autoimmune, viral, infectious or genetic factors have been suggested. The estimated annual incidence rate is around 5-10 cases/1,000,000 in the United States; it increases with age, with the highest rates seen in the 35-44 and 55-64 years. Women are two times more likely to suffer from PM than men. Corticosteroids and immunosuppressant agents are the mainstay of treatment, with a significant percentage of non-responders and clinical relapses [105]. Hematopoietic stem cell transplantation is performed in patients with refractory PM with satisfactory clinical efficacy [106], but the condition regimen for the procedure has many side effects. Allogeneic MSCs from bone marrow and umbilical cord were transplanted in 10 patients with drug-resistant PM [107]. Although none of the patients stopped immunosuppressive therapy for more than 1-year's follow-up and there was no cure, MSCs treatment may prove to be a useful adjunctive treatment in patients whose disease is poorly controlled with immunosuppressive agents.						

3	35/F	4x each $5x10^8$ (i.v.)	$2x10^9$	inability to walk slope and to stand up by herself	Able to step up stairs (< 10 cm) and walk gentle slope holding handrail	3
Atopic Dermatitis AD is a common, chronic and refractory skin disease manifesting as eczema and pruritus with repeated exacerbations and regressions and unknown pathogenesis [108]. The incidence of AD in adults has increased worldwide over the past decade [109]. Current management aims to relieve frequency of dermal inflammation and prevent its flare-up using topical corticosteroids and tacrolimus [109,110]. Although these treatments might control the symptoms, relapse is frequent and extensive and prolonged use of corticosteroid carries risk of side-effects, including skin atrophy and there are many AD patients with corticosteroid phobia [111]. Despite the immunomodulating effect of MSC, there is no previous record of stem cell treatment of AD.						
4	27/F	3x each $2x10^8$ (i.v.)	$6x10^8$	SCORAD index 93.1	SCORAD* index 61.1	5.5
5	33/M	3x each $2x10^8$ (i.v.)	$6x10^8$	SCORAD index 57.0	SCORAD index 35.5	4.5
6	27/F	5x each $2x10^8$ (i.v.)	$1x10^9$	SCORAD index 33.4	SCORAD index 16.4	3.5
7	26/F	3x each $2x10^8$ (i.v.)	$6x10^8$	SCORAD index 39.1	SCORAD index 13.3	2
Rheumatoid Arthritis RA is a T-cell-mediated systemic autoimmune disease caused by loss of immunologic self tolerance and characterized by synovium inflammation and articular destruction. MSCs were reported to reduce inflammatory and T cell responses and induce antigen specific regulatory T cells in vitro in rheumatoid arthritis [114]. Systemic infusion of hAdMSCs significantly reduced the incidence and severity of experimental arthritis induced by CIA in vivo [115], which was mediated by down-regulating Th1-driven autoimmune and inflammatory responses and induction of interleukin-10 in lymph nodes and joints. Human AdMSCs also induced de novo generation of antigen-specific CD4+CD25+FoxP3+ Treg cells. The best therapeutic benefits were seen when the stem cell treatments were performed prior to onset and by systemic rather than local application. Recently, the therapeutic effects of systemic infusion human umbilical cord (UC)-MSCs were also verified in the collagen-induced arthritis model [116] with effects similar to those of hAdMSCs.						
8	50/F	2x each $3x10^8$ (i.v.)	$6x10^8$	***VAS score: 10 KWOMAC score: 73	VAS score:2-3 KWOMAC score: 28	7
9	51/F	Once $2x10^8$ (i.v.) + $1x10^8$ (intrarticular) Once $3.5x10^8$ (i.v.) + $1.5x10^8$ (intrarticular))	$8x10^8$	Inability to stand up, crutches for walking	Ability to stand up, off steroids	3
10	67/M	4x each $2x10^8$ (i.v.)	$8x10^8$	Inability to walk	Normal walking, off steroids	13

Table 1. Results of SCORing Atopic Dermatitis (SCORAD) index in atopic dermatitis patients before and after the stem cells treatment (see also supplementary information).

Patient	Gender	Age	Total cell dose	Injection Route	Follow-up (months)	Extent		Intensity		Pruritus / Insomnia		Total score	
						Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	F	27y	$6x10^8$	Intravenous	5½	98	98	17	11	14	3	93.1	61.1
2	M	33y	$6x10^8$	Intravenous	4½	75	75	7	5	14	3	57	35.5
3	F	27y	$1x10^9$	Intravenous	3½	12	7	8	4	3	1	33.4	16.4
4	F	26y	$6x10^8$	Intravenous	2	18	4	7	3	11	2	39.1	13.3