toxicity from infusion of FMCs. Two of eight evaluable patients had a complete response and four had a partial response, giving an overall response rate of 75%. Three patients are alive from 6 to 21 months after HSCT. One patient is well and two have chronic GVHD. Two patients showed no response at all.

Thus, FMCs may be successfully used for immune modulation and tissue repair.

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α-Mannan Can Induce Acute Pulmonary GvHD Dependent On Th17 Subsets

Hidetaka Uryu [1], Hideyo Oka [1], Sonoko Shimoji [1], Yoshihiro Eriguchi [1], Shuichiro Takashima [1], Koji Kato [1], Koichi Akashi [1], Takanori Teshima [2]. [1] Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Science, Japan; [2] Department of Hematology, Hokkaido University Graduate School of Medicine, Sapporo-City, Japan

Fungal infection is a serious complication after allogeneic hematopoietic stem cell transplantation but its impacts on graft-versus host disease (aGVHD) remains to be elucidated. α-mannan, one of the main components of fungal cell wall, induces Th17 responses, leading to the elimination of fungi. We therefore hypothesized that fungal infection could modulate GVHD by inducing Th17 responses. Lethally irradiated B6D2F1 (H-$2^{b/d}$) mice were injected with 4 x 10^6 BM and 4 x 10^6 T cells from MHC-mismatched B6 (H-2^b) donors on day 0. Mice were intraperitoneally injected with 20mg of α-mannan or diluent on day 1. GVHD was severe in mannan-treated allogeneic mice, with 16.7% survival by day30, whereas 83.3% of allogeneic controls survived this period (Table). Histopathologic examination showed significantly exacerbation of GVHD pathology, especially in the lung, of mannan-treated animals than in controls (Table).

A flowcytometric analysis of the spleen and thymus after BMT showed that administration of mannan did not alter donor cell engraftment.

We then evaluated the roles of Th17 in aGVHD of mannan-treated allogeneic models using IL-17-deficient mice as donors. Infusion of IL-17-/- T cells significantly improved GVHD clinical scores (3.5 ± 0.4 vs 5.5±0.3 at day14, P<.05), survival (62.5% vs 12.5% at day 30, $P < .05$) and pulmonary GVHD pathology scores (1.0±0.5 vs 7.0±1.0 at day21, $P < .05$) compared with those of mannan-treated controls.

These results suggest that mannan can exacerbate acute GVHD, mainly on pulmonary lesions.Th17 contribute to the development of acute pulmonary GVHD in this model, and that targeting Th17 may therefore represent a promising therapeutic strategy for treating acute pulmonary GVHD.

Table

Group	Clinical GVHD scores on day+14	Survivals on day+30 (%)	Pathology Scores		
			Lung	Liver	Intestine
TCD Diluent	1.1±0.8	100	0	0.3±0.4	0.7±0.4
TCD α-mannan	1.2±0.5	100	0	0.7±0.8	0.5±0.5
+T Diluent	3.6±0.7	83.3	1.5±0.7	2.5± 1.2	2.0± 0.8
+T α-mannan	5.7±0.5†	16.7*	7.0±1.0†	4.0± 1.8	2.5± 0.8

TCD: T cell-depleted BMT, +T: T cell-repleted BMT.
Data are expressed as mean ± SD.
* $P < 0.01$ vs control.
† P<0.05 vs control.

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Plasma ST2 Concentrations Predict Acute Gvhd Development and Non-Relapse Mortality

Mark Vander Lugt [1], Thomas Braun [2], Samir Hanash [3], James L.M. Ferrara [1], Jerome Ritz [4], Vincent T. Ho [5], Joseph H. Antin [5], Qing Zhang [3], Alice Chin [3], Aurelie Gomez [1], Andrew C. Harris [1], John E. Levine [1], Sung Won Choi [1], Daniel R. Couriel [2], Pavan Reddy [1], Sophie Paczesny [2]. [1] University of Michigan, Ann Arbor, MI; [2] Blood and Marrow Transplant Program, University of Michigan, Ann Arbor, MI; [3] Fred Hutchinson Cancer Research Center, Seattle, WA; [4] Dana-Farber Cancer Institute, Boston, MA; [5] Hematologic Malignancies, Dana-Farber Cancer Institute, Boston, MA

Acute GVHD is the primary limitation of allogeneic HSCT. We have previously reported that plasma concentrations of suppressor of tumorigenicity 2 (ST2) at the onset of GVHD therapy predicted response at day (D) 28 and non-relapse mortality (NRM) at D180 after therapy initiation. We hypothesized that ST2 measured early in HSCT would predict GVHD occurrence by D100 and D180 NRM after HSCT.

We measured ST2 in plasma taken at D0, D14 and D21 after HSCT in a pilot set. ST2 concentrations at D14 were most different between patients who developed GVHD and those without GVHD, and were twice higher in patients receiving full intensity conditioning (FIC) compared to those receiving reduced intensity conditioning (RIC). We then measured ST2 concentrations at D14 in two independent sets: 1) 598 patients from the University of Michigan (UM), 69% receiving FIC (15% receiving TBI) and 31% receiving RIC HSCT, 2) 75 patients receiving unrelated, FIC (92% receiving TBI) HSCT from the Dana Farber Cancer Institute (DFCI). UM patients who developed GVHD were older and more likely to receive mismatched or unrelated donor HSCT. Median day of GVHD onset was D35 in FIC and D42 in RIC (p=0.08). DFCI patients who received sirolimus as GVHD prophylaxis were over-

Table 1
ST2 concentrations at D14 predict GVHD development by D100 and predict D180 NRM

	UM FIC (n = 414)		UM RIC (n = 184)		DFCI (n = 75)	
	Hazard Ratio (HR)	*P*-value	HR	*P*-value	HR	*P*-value
Age (55 and Over vs. Under 55)	1.5	0.01	0.8	0.4	0.1	0.02
Disease Status (High vs. Low risk)	1.0	0.99	1.8	0.02		n/a
Donor (Unrelated vs. Related)	1.9	<0.001	0.9	0.7		n/a
HLA match (Mismatched vs. Matched)	2.1	<0.001	1.0	0.9	2.7	0.09
ST2 Concentration (High vs. Low)*,†	1.5	0.004	1.3	0.3	2.0	0.08
Age	3.1	<0.001	0.7	0.4	0.7	0.5
Disease Status	1.1	0.6	2.7	0.02		n/a
Donor	1.5	0.1	1.1	0.8		n/a
HLA match	1.7	0.06	0.5	0.3	1.9	0.2
ST2 Concentration	2.8	<0.001	4.8	0.005	2.6	0.04

* Effect of ST2 calculated with regression models adjusting for age, disease status, donor, and HLA match.
† High defined as ST2 concentration >600 pg/mL for UM FIC, >300 pg/mL for UM RIC, >1660 pg/mL for DFCI.