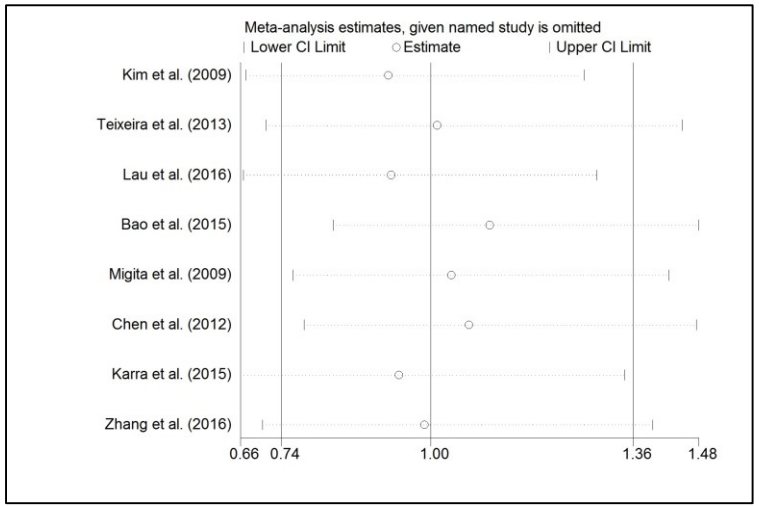
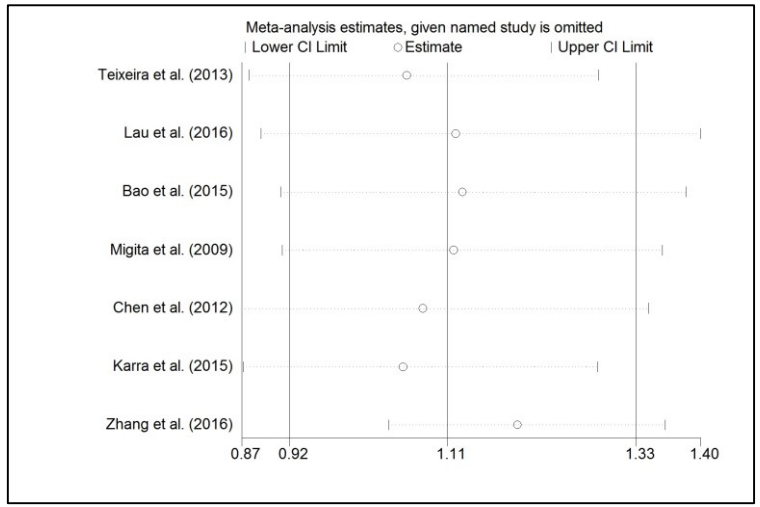
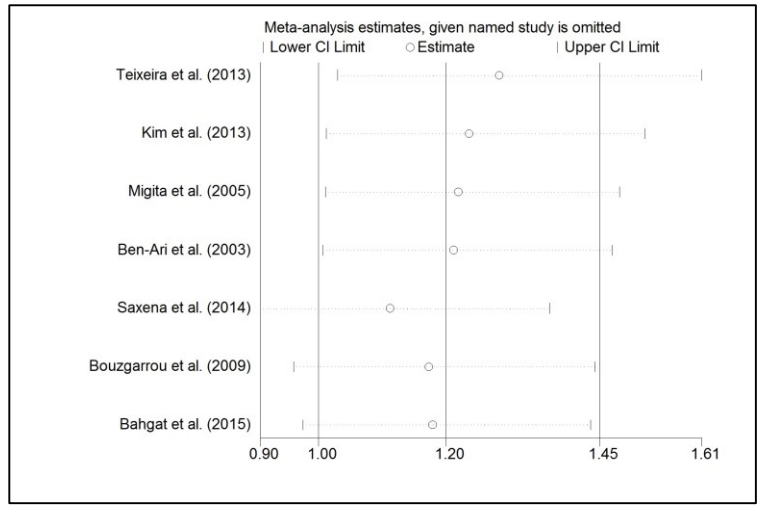


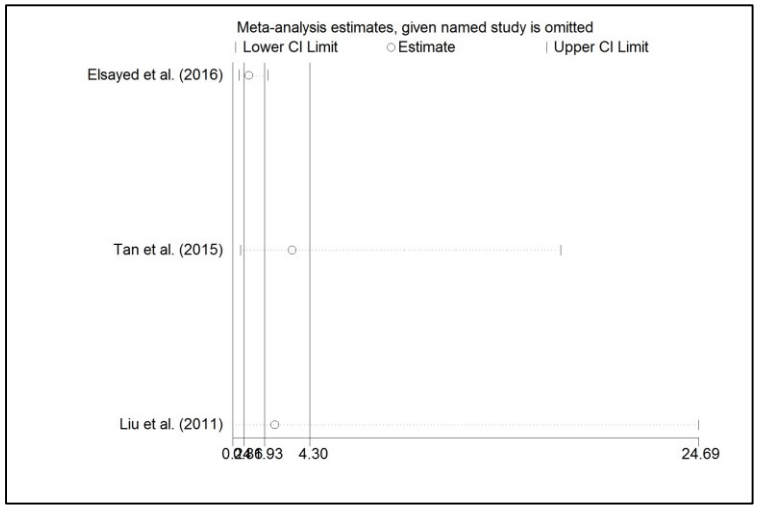
IL18 rs187238



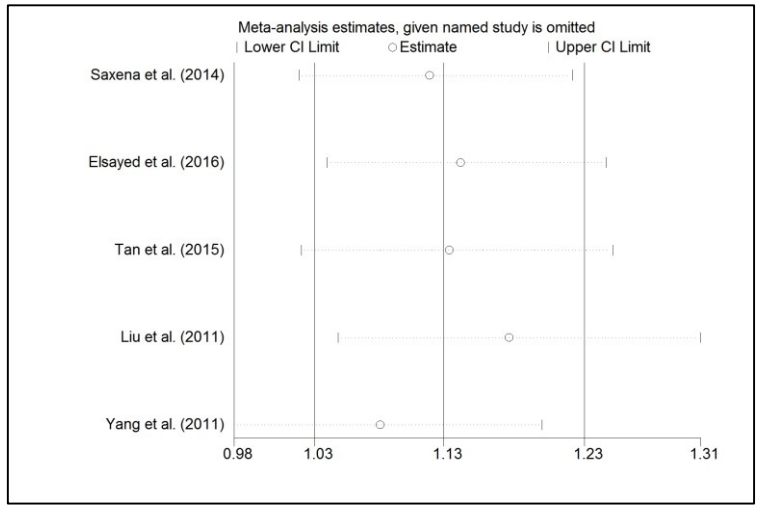
IL18 rs1946518



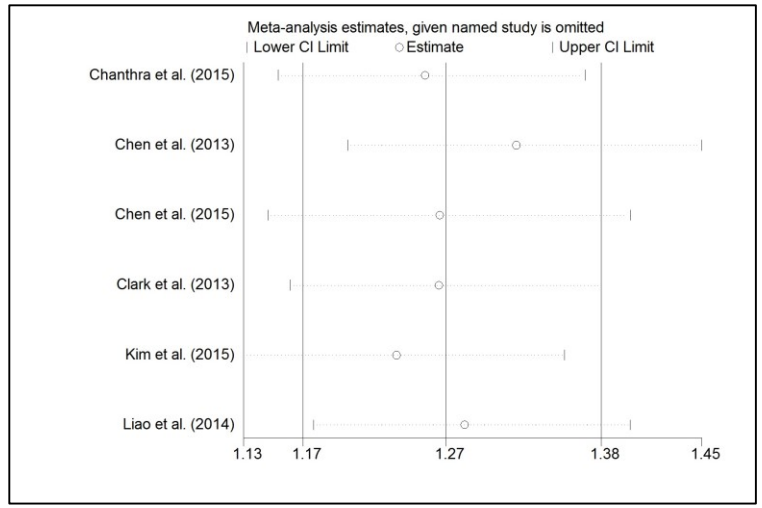
IFN-γ rs2430561



IL12A rs568408

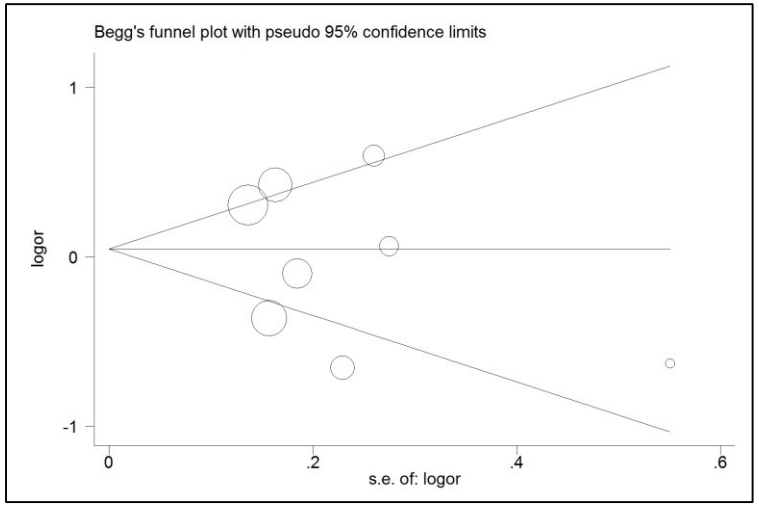


IL12B rs3212227

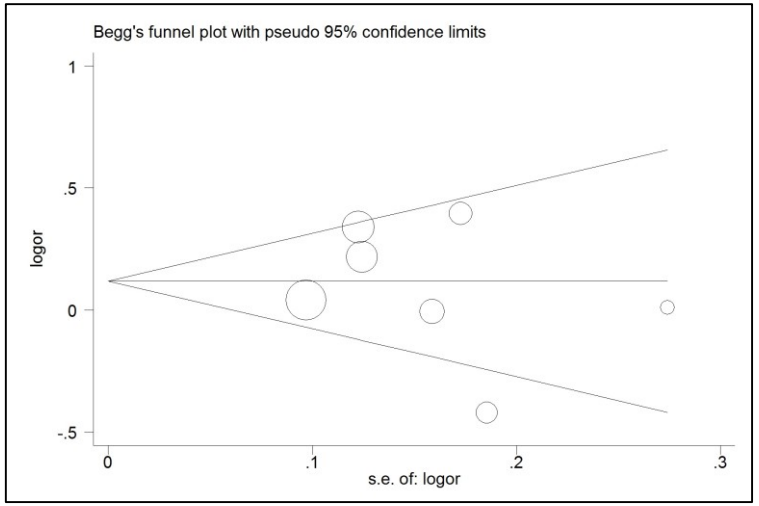


STAT4 rs7574865

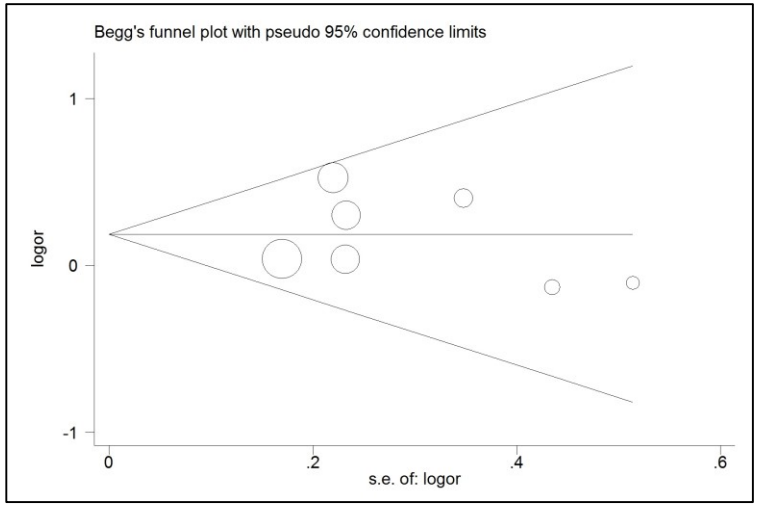
Supplementary figure 1. Sensitivity Analysis of Overall OR Co-Efficients for 6 polymorphisms of IL-12 pathway genes (M vs. W). Results were calculated by omitting each study in turn. The two ends of the dotted lines represent the 95% CI.



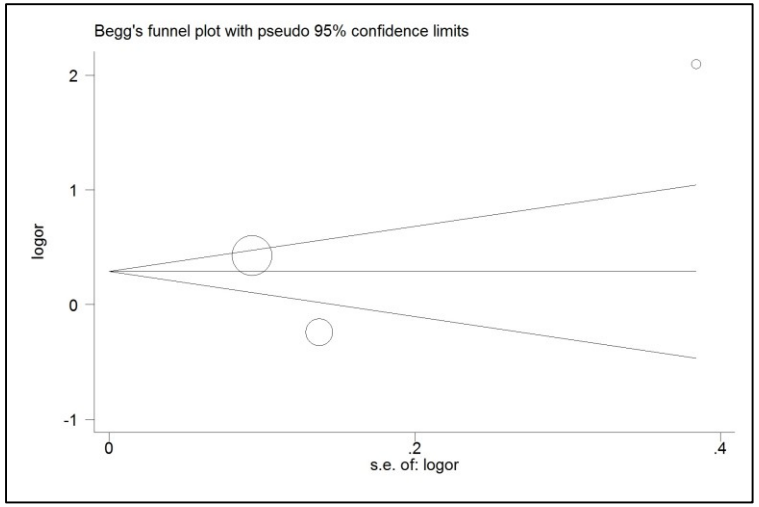
IL18 rs187238



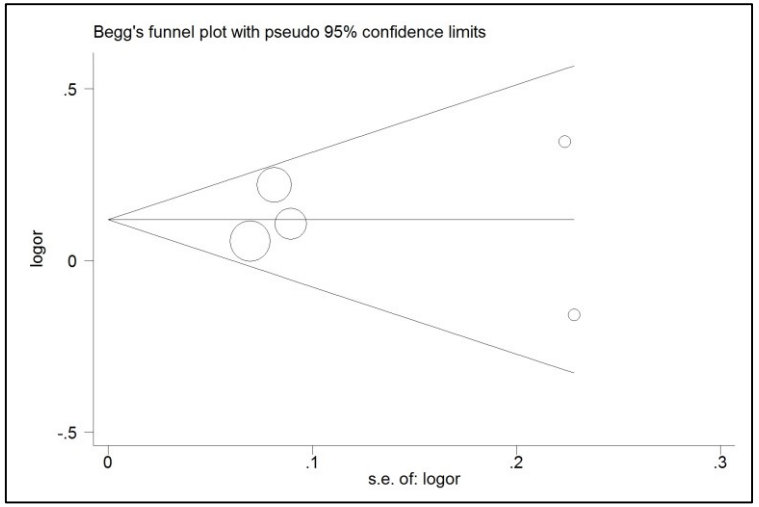
IL18 rs1946518



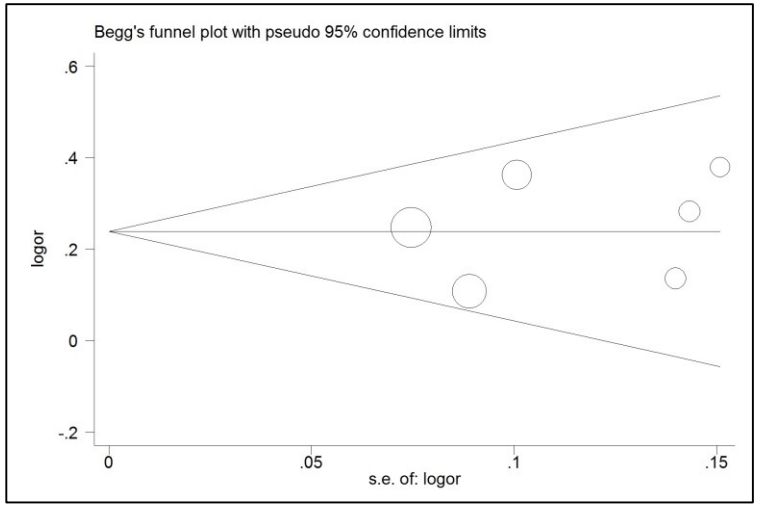
IFN-γ rs2430561



IL12A rs568408



IL12B rs3212227



STAT4 rs7574865

Supplementary figure 2. Begg's funnel plot for publication bias test under 6 polymorphisms of IL-12 pathway gene (M vs. W). The x-axis is log (OR), and the y-axis is natural logarithm of OR. The horizontal line in the figure represents the overall estimated log (OR). The two diagonal lines indicate the pseudo 95% confidence limits of the effect estimate. Log (OR) = log-transformed OR, OR = odds ratio.

Table S1. The NOS quality control of enrolled studies.

Variants	Author	Adequacy of Case Definition	Representativeness of the Cases	Selection of Controls	Definition of Controls	Comparability Cases/Controls	Ascertainment	Same Method of Ascertainment	Non-response rate
rs1946518	Teixeira *et al.*	*	*	*	*	**	*	*	NA
	Lau *et al.*	*	*	NA	*	*	NA	*	NA
	Bao *et al.*	*	*	*	*	**	*	*	NA
	Migita *et al.*	*	*	*	*	**	*	*	NA
	Chen *et al.*	*	*	*	*	**	NA	*	NA
	Karra *et al.*	*	*	*	*	*	*	*	NA
	Zhang *et al.*	*	*	*	*	*	*	*	NA
	Kim *et al.*	*	*	NA	NA	**	*	*	NA
rs187238	Teixeira *et al.*	*	*	*	*	**	*	*	NA
	Lau *et al.*	*	*	NA	*	*	NA	*	NA
	Bao *et al.*	*	*	*	*	**	*	*	NA
	Migita *et al.*	*	*	*	*	**	*	*	NA
	Chen *et al.*	*	*	*	*	**	NA	*	NA
	Karra *et al.*	*	*	*	*	*	*	*	NA
	Zhang *et al.*	*	*	*	*	*	*	*	NA

	Teixeira *et al.*	*	*	*	*	**	*	*	NA
	Kim *et al.*	*	*	NA	*	*	*	*	NA
	Migita *et al.*	*	*	NA	*	*	*	*	NA
	Ben-Ari *et al.*	*	*	*	*	*	*	*	NA
rs2430561	Nieters *et al.*	*	*	NA	*	**	NA	*	NA
	Saxena *et al.*	*	*	*	NA	*	*	*	NA
	Bouzgarrou *et al.*	*	*	*	*	*	*	*	NA
	Bahgat *et al.*	*	*	*	*	*	*	*	NA
	Heba Mosaad Elsayed *et al.*	*	*	*	*	**	*	*	NA
rs568408	Tan *et al.*	*	*	*	*	**	*	*	NA
	Liu *et al.*	*	*	*	*	**	*	*	NA
	Saxena *et al.*	*	*	*	*		*	*	NA
	Heba Mosaad Elsayed *et al.*	*	*	*	*	**	*	*	NA
	Alexandra Nieters *et al.*	*	*	*	*	*	NA	*	NA
rs3212227	Tan *et al.*	*	*	*	*	**	*	*	NA
	Simona Ognjanovic *et al.*	*	*	*	*	**	NA	*	NA
	Liu *et al.*	*	*	*	*	**	*	*	NA

rs7574865	Yang *et al.*	*	*	NA	*	**	*	*	NA
	Chanthra *et al.*	*	*	*	*	*	*	*	NA
	Chen *et al.*	*	*	NA	*	**	*	*	NA
	Chen *et al.*	*	*	*	*	**	*	*	NA
	Clark *et al.*	*	*	NA	*	*	*	*	NA
	Kim *et al.*	*	*	*	*	*	NA	*	NA
	Liao *et al.*	*	*	*	*	*	*	*	NA

NA: not mentioned.

Table S2. Sensitivity analysis for current meta-analysis.

Polymorphism	Comparison	Study omitted	Estimate	95%CI	Effect Model
		Teixeira *et al.*	1.060	0.875-1.285	
		Lau *et al.*	1.117	0.889-1.404	
		Bao *et al.*	1.125	0.912-1.387	
	M VS. W	Migita *et al.*	1.115	0.914-1.360	Random
		Chen *et al.*	1.079	0.867-1.343	
		Karra *et al.*	1.055	0.868-1.283	
		Zhang *et al.*	1.190	1.038-1.363	
rs1946518		Teixeira *et al.*	1.123	0.751-1.679	
		Lau *et al.*	1.307	0.766-2.231	
		Bao *et al.*	1.323	0.809-2.161	
	MM vs. WW	Migita *et al.*	1.304	0.826-2.059	Random
		Chen *et al.*	1.211	0.730-2.008	
		Karra *et al.*	1.150	0.728-1.818	
		Zhang *et al.*	1.480	1.044-2.099	
	WM vs. WW	Teixeira *et al.*	1.152	0.900-1.473	Random

	Lau *et al.*	1.206	0.939-1.549	
	Bao *et al.*	1.172	0.921-1.491	
	Migita *et al.*	1.149	0.914-1.445	
	Chen *et al.*	1.113	0.880-1.408	
	Karra *et al.*	1.086	0.884-1.335	
	Zhang *et al.*	1.233	1.029-1.479	
	Teixeira *et al.*	1.135	0.850-1.515	
	Lau *et al.*	1.203	0.887-1.633	
	Bao *et al.*	1.194	0.895-1.592	
MM+MW vs. WW	Migita *et al.*	1.169	0.888-1.538	Random
	Chen *et al.*	1.121	0.839-1.497	
	Karra *et al.*	1.095	0.844-1.420	
	Zhang *et al.*	1.283	1.080-1.524	
	Teixeira *et al.*	1.062	0.833-1.353	
	Lau *et al.*	1.179	0.797-1.744	
MM vs. MW+WW	Bao *et al.*	1.199	0.843-1.707	Random
	Migita *et al.*	1.191	0.864-1.642	

rs187238	M VS. W	Chen *et al.*	1.140	0.787-1.651	Random
		Karra *et al.*	1.086	0.779-1.515	
		Zhang *et al.*	1.263	0.958-1.665	
		Kim *et al.*	0.926	0.674-1.272	
		Teixeira *et al.*	1.013	0.709-1.447	
		Lau *et al.*	0.931	0.669-1.294	
		Bao *et al.*	1.106	0.828-1.476	
		Migita *et al.*	1.038	0.757-1.423	
	MM vs. WW	Chen *et al.*	1.069	0.776-1.471	Random
		Karra *et al.*	0.945	0.664-1.345	
		Zhang *et al.*	0.990	0.703-1.394	
		Kim *et al.*	0.920	0.600-1.408	
		Teixeira *et al.*	1.145	0.658-1.994	
		Lau *et al.*	1.037	0.596-1.805	
		Bao *et al.*	1.113	0.666-1.861	
		Migita *et al.*	1.034	0.612-1.748	
		Chen *et al.*	1.081	0.591-1.979	

	Karra *et al.*	0.951	0.53-1.704	
	Zhang *et al.*	1.084	0.64-1.836	
	Kim *et al.*	0.917	0.588-1.432	
	Teixeira *et al.*	0.977	0.61-1.565	
	Lau *et al.*	0.899	0.577-1.402	
	Bao *et al.*	1.117	0.757-1.65	
WM vs. WW	Migita *et al.*	1.049	0.694-1.586	Random
	Chen *et al.*	1.099	0.742-1.627	
	Karra *et al.*	0.904	0.574-1.424	
	Zhang *et al.*	0.950	0.604-1.496	
	Kim *et al.*	0.913	0.601-1.389	
	Teixeira *et al.*	0.993	0.633-1.559	
	Lau *et al.*	0.909	0.594-1.392	
MM+MW vs. WW	Bao *et al.*	1.120	0.773-1.623	Random
	Migita *et al.*	1.047	0.702-1.563	
	Chen *et al.*	1.090	0.740-1.606	
	Karra *et al.*	0.914	0.592-1.409	

	MM vs. MW+WW	Zhang *et al.*	0.967	0.625-1.495	Random
		Kim *et al.*	0.912	0.600-1.388	
		Teixeira *et al.*	1.122	0.705-1.786	
		Lau *et al.*	1.024	0.632-1.659	
		Bao *et al.*	1.062	0.607-1.684	
		Migita *et al.*	1.012	0.639-1.603	
		Chen *et al.*	1.000	0.590-1.696	
		Karra *et al.*	0.991	0.578-1.700	
	M VS. W	Zhang *et al.*	1.056	0.672-1.659	Fixed
		Teixeira *et al.*	1.230	1.023-1.479	
		Kim *et al.*	1.204	1.013-1.431	
		Migita *et al.*	1.195	1.014-1.409	
		Ben-Ari *et al.*	1.190	1.010-1.401	
rs2430561		Nieters *et al.*	1.202	0.998-1.448	
		Saxena *et al.*	1.115	0.937-1.327	
		Bouzgarrou *et al.*	1.159	0.975-1.377	
		Bahgat *et al.*	1.165	0.986-1.375	

MM vs. WW	Teixeira *et al.*	2.212	1.320-3.705	Fixed
	Kim *et al.*	1.557	1.029-2.354	
	Migita *et al.*	1.630	1.094-2.428	
	Ben-Ari *et al.*	1.683	1.123-2.523	
	Nieters *et al.*	1.630	1.094-2.428	
	Saxena *et al.*	1.372	0.875-2.150	
	Bouzgarrou *et al.*	1.613	1.025-2.538	
	Bahgat *et al.*	1.581	1.045-2.393	
WM vs. WW	Teixeira *et al.*	1.035	0.813-1.317	Fixed
	Kim *et al.*	1.126	0.886-1.431	
	Migita *et al.*	1.078	0.860-1.351	
	Ben-Ari *et al.*	1.051	0.842-1.311	
	Nieters *et al.*	1.014	0.772-1.333	
	Saxena *et al.*	1.045	0.830-1.314	
	Bouzgarrou *et al.*	1.082	0.861-1.358	
	Bahgat *et al.*	1.067	0.854-1.333	
MM+MW vs. WW	Teixeira *et al.*	1.131	0.895-1.429	Fixed

		Kim *et al.*	1.185	0.940-1.493	
		Migita *et al.*	1.152	0.927-1.430	
		Ben-Ari *et al.*	1.127	0.912-1.394	
		Nieters *et al.*	1.121	0.867-1.449	
		Saxena *et al.*	1.088	0.871-1.358	
		Bouzgarrou *et al.*	1.132	0.908-1.411	
		Bahgat *et al.*	1.128	0.911-1.397	
		Teixeira *et al.*	2.155	1.381-3.363	
	MM vs. MW+WW	Kim *et al.*	1.502	1.049-2.150	Fixed
		Migita *et al.*	1.564	1.104-2.216	
		Ben-Ari *et al.*	1.624	1.140-2.313	
		Nieters *et al.*	1.564	1.104-2.216	
		Saxena *et al.*	1.351	0.912-2.001	
		Bouzgarrou *et al.*	1.488	0.998-2.220	
		Bahgat *et al.*	1.492	1.035-2.150	
rs568408	M VS. W	Elsayed *et al.*	1.105	0.573-2.130	Random
		Tan *et al.*	3.387	0.658-17.429	

		Liu *et al.*	2.458	0.245-24.688	
		Elsayed *et al.*	1.404	0.384-5.130	
	MM vs. WW	Tan *et al.*	5.738	0.800-41.130	Random
		Liu *et al.*	3.304	0.111-98.066	
		Elsayed *et al.*	1.112	0.552-2.242	
	WM vs. WW	Tan *et al.*	3.203	0.704-14.572	Random
		Liu *et al.*	2.294	0.248-21.224	
		Elsayed *et al.*	1.123	0.538-2.345	
	MM+MW vs. WW	Tan *et al.*	3.629	0.677-19.444	Random
		Liu *et al.*	2.538	0.225-28.688	
		Elsayed *et al.*	1.356	0.450-4.085	
	MM vs. MW+WW	Tan *et al.*	4.244	0.788-22.861	Random
		Liu *et al.*	2.731	0.146-50.933	
		Saxena *et al.*	1.126	1.039-1.221	
		Elsayed *et al.*	1.145	1.056-1.242	
rs3212227	M VS. W				Fixed
		Nieters *et al.*	1.134	1.043-1.232	
		Tan *et al.*	1.140	1.043-1.247	

	Ognjanovic *et al.*	1.128	1.040-1.224	
	Liu *et al.*	1.176	1.066-1.297	
	Yang *et al.*	1.100	1.003-1.206	
	Saxena *et al.*	1.257	1.052-1.501	
	Elsayed *et al.*	1.291	1.080-1.543	
	Nieters *et al.*	1.277	1.072-1.520	
MM vs. WW	Tan *et al.*	1.287	1.053-1.572	Fixed
	Ognjanovic *et al.*	1.277	1.072-1.520	
	Liu *et al.*	1.401	1.119-1.752	
	Yang *et al.*	1.177	0.956-1.448	
	Saxena *et al.*	1.167	1.026-1.328	
	Elsayed *et al.*	1.213	1.067-1.380	
	Nieters *et al.*	1.155	1.011-1.319	
WM vs. WW	Tan *et al.*	1.191	1.036-1.300	Fixed
	Ognjanovic *et al.*	1.158	1.015-1.321	
	Liu *et al.*	1.209	1.036-1.412	
	Yang *et al.*	1.148	0.994-1.325	

		Saxena *et al.*	1.193	1.056-1.349	
		Elsayed *et al.*	1.238	1.094-1.400	
		Nieters *et al.*	1.188	1.047-1.348	
	MM+MW vs. WW	Tan *et al.*	1.218	1.066-1.392	Fixed
		Ognjanovic *et al.*	1.190	1.050-1.349	
		Liu *et al.*	1.256	1.083-1.457	
		Yang *et al.*	1.163	1.013-1.335	
		Saxena *et al.*	1.163	0.998-1.355	
		Elsayed *et al.*	1.170	1.003-1.364	
		Nieters *et al.*	1.175	1.010-1.367	
	MM vs. MW+WW	Tan *et al.*	1.180	0.991-1.405	Fixed
		Ognjanovic *et al.*	1.175	1.010-1.367	
		Liu *et al.*	1.272	1.049-1.541	
		Yang *et al.*	1.114	0.930-1.335	
		Chanthra *et al.*	1.257	1.152-1.371	
rs7574865	M VS. W	Chen *et al.*	1.322	1.202-1.454	Fixed
		Chen *et al.*	1.267	1.145-1.403	

MM vs. WW	Clark *et al.*	1.266	1.160-1.382	Fixed
	Kim *et al.*	1.236	1.127-1.356	
	Liao *et al.*	1.285	1.177-1.403	
	Chanthra *et al.*	1.626	1.320-2.002	
	Chen *et al.*	1.718	1.372-2.152	
	Chen *et al.*	1.639	1.288-2.086	
	Clark *et al.*	1.636	1.326-2.017	
	Kim *et al.*	1.607	1.291-2.001	
	Liao *et al.*	1.725	1.396-2.131	
WM vs. WW	Chanthra *et al.*	1.307	1.058-1.614	Fixed
	Chen *et al.*	1.273	1.015-1.596	
	Chen *et al.*	1.278	1.002-1.629	
	Clark *et al.*	1.279	1.035-1.58	
	Kim *et al.*	1.312	1.053-1.635	
	Liao *et al.*	1.363	1.100-1.688	
MM+MW vs. WW	Chanthra *et al.*	1.465	1.198-1.791	Fixed
	Chen *et al.*	1.485	1.197-1.842	

	Chen *et al.*	1.450	1.150-1.827	
	Clark *et al.*	1.451	1.186-1.775	
	Kim *et al.*	1.452	1.177-1.791	
	Liao *et al.*	1.539	1.255-1.887	
	Chanthra *et al.*	1.297	1.159-1.451	
	Chen *et al.*	1.409	1.244-1.595	
MM vs. MW+WW	Chen *et al.*	1.322	1.157-1.510	Fixed
	Clark *et al.*	1.320	1.179-1.479	
	Kim *et al.*	1.269	1.124-1.432	
	Liao *et al.*	1.327	1.184-1.486	

CI: confidential interval

Table S3. Egger's regression test for polymorphisms in genes of IL-12 signaling pathway

Gene	Polymorphism	Egger's test
		P **> |t|**
IL18	rs1946518	0.621
IL18	rs187238	0.551
IFN-γ	rs2430561	0.824
IL12A	rs568408	0.673
IL12B	rs3212227	0.999
STAT4	rs7574865	0.651