Supplemental Table S1. Characteristics of strains and their mutant derivatives used in this study

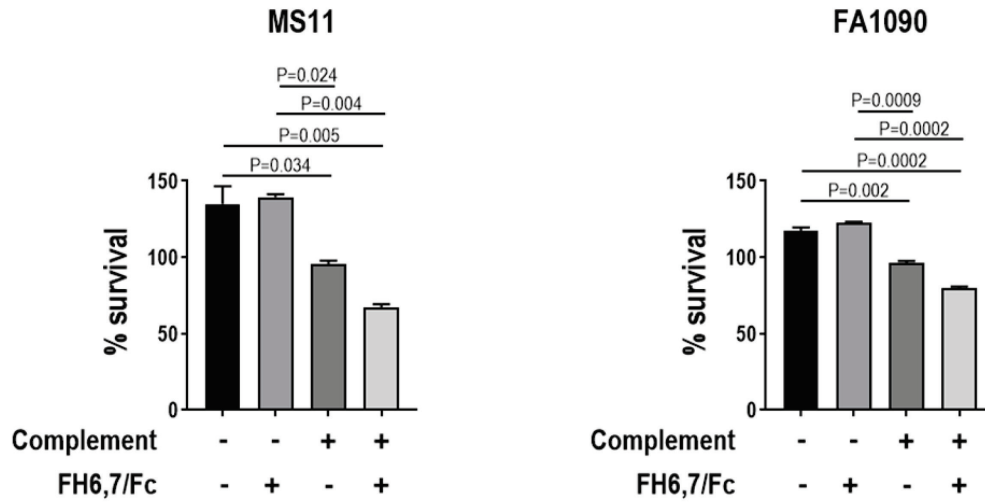| Strain	Characteristics
F62	Isolated in 1962 (Atlanta, USA); Proline auxotroph; Expresses PorB.1B
F62 ΔlgtA	F62 *lgtA::kan^R*; LOS expresses lactose from HepI
Ctx-r(Spain)	Isolated in Spain. CRO-R (CRO MIC 1.5 µg/ml); NG-MAST sequence type 1407
Ctx-r(Spain) ΔlgtA	Ctx-r(Spain) *lgtA::kan^R*
H041	Isolated in Japan; CRO-R (CRO MIC 2-4 µg/ml); NG-MAST sequence type ST4220; MLST sequence type ST7363
H041 ΔlgtA	H041 *lgtA::kan^R*
MS11	Isolated in 1970 form male with uncomplicated urethritis; PorB.1B-9; has been used in human male volunteer model of gonorrhea.
MS11 ΔlgtA	MS11 *lgtA::kan^R*
MS11 Opa-	MS11 with all 11 opa genes deleted
UMNJ60_06UM (NJ-60)	Isolated from endocervix in Nanjing, China (2013).
UMNJ60_06UM ΔlgtA	UMNJ60_06UM *lgtA::kan^R*
FA1090	Isolated from endocervix of a woman with probable disseminated gonococcal infection in the 1970s; PorB.1B-3; used in human male volunteer model of gonorrhea
FA1090 ΔlgtA	FA1090 *lgtA::kan^R*
FA1090 Opa-	FA1090 with all 11 opa genes deleted

CRO-R, ceftriaxone resistant; MIC, minimum inhibitory concentration; NG-MAST, *Neisseria gonorrhoeae* multi-antigen sequence typing; MLST, multi-locus sequence typing; Por, Porin; lgt, LOS glycosyltransferase; Opa, Opacity protein

Supplemental Table S2. Characteristics of GISP strains used in this study

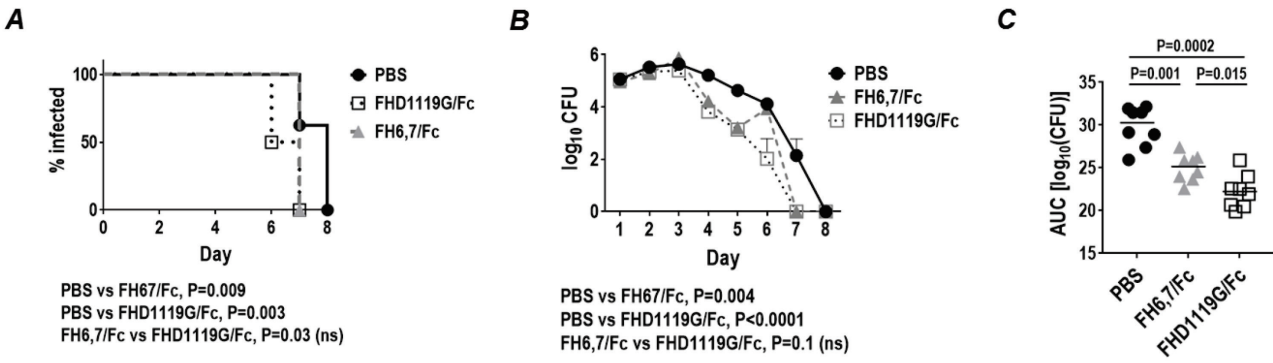| Study Site	Study Month	Study Number	MIC A (µg/ml; Etest)			NG-MAST	PorB Allele	TbpB Allele	PenA Genotype
			CRO	CFX	AZI				
OC	2	14	0.064	0.016	0.19	3307	30	743	non-mosaic
OC	12	7	0.032	0.016	1	8535	4760	4	non-mosaic
SD	11	3	0.032	0.032	0.25	2400	1489	563	non-mosaic
SD	5	5	0.094	0.125	0.5	1407	908	110	XXXIV
SD	7	8	0.064	0.032	0.25	2400	1489	563	non-mosaic
SD	1	15	0.094	0.125	0.38	1407	908	110	XXXIV
SF	12	2	0.047	0.125	0.38	1407	908	110	XXXIV
SF	7	6	0.008	0.016	0.125	8424	292	743	non-mosaic
SF	7	7	0.006	<0.016	0.38	8481	4883	29	non-mosaic

OC, Orange County; SD, San Diego; SF, San Francisco; MIC, Minimum Inhibitory Concentration; CRO, ceftriaxone; CFX, cefixime; AZI, azithromycin; NG-MAST, *Neisseria gonorrhoeae* Multi-Antigen Sequence Typing; PorB, Porin B; TbpB, Transferrin binding protein B

Supplemental Figure S1. Opsonophagocytic killing of Opa-negative mutants of *N. gonorrhoeae* MS11 and FA1090 by FH6,7/Fc and complement. Opa-negative MS11 (left graph) and FA1090 (right graph) were incubated with FH6,7/Fc (67 µg/ml) and 10% (v/v) human complement (IgG and IgM depleted normal human serum), followed by the addition of 10^6 freshly isolated human PMNs (multiplicity of infection 1:1) for 60 min at 37˚C. Bacterial survival at 60 min relative to 0 min is shown on the Y-axis (mean [range] of two independently performed experiments). Controls included reactions where complement and/or FH6,7/Fc was omitted. Comparisons across groups was made by one-way ANOVA (P=0.003 for MS11 and P=0.0001 for FA1090) and pairwise comparisons (indicated with the graphs) by Tukeys multiple comparisons test.

Supplemental Figure S2. Efficacy of FH6,7/Fc and FHD1119G/Fc against FA1090 in the mouse vaginal colonization model using FH/C4BP dual transgenic (Tg) mice. Premarin®-treated FH/C4BP dual Tg mice (n=8/group) were given 7 x 10^7 CFU strain FA1090 intravaginally on Day 0 and treated intravaginally daily with 10 μg/d of either FH6,7/Fc (dashed grey lines and triangles) or FHD1119G/Fc (dotted black lines and non-filled squares) or 10 μl/d PBS (control; solid black line and circles) from Day 0 to Day 8. Vaginas were swabbed daily to enumerate CFU. *A*. Kaplan Meier curves showing time to clearance of infection. Groups were compared using the log-rank (Mantel-Cox) test. Significance was set at 0.017 (Bonferroni's correction for comparisons across three groups). *B*. Log_{10} CFU versus time. X-axis, day; Y-axis, log_{10} CFU. *C*. Bacterial burdens consolidated over time (Area Under the Curve [log_{10} CFU] analysis) for the two groups. The three groups were comparisons using the non-parametric Kruskal-Wallis equality of populations rank test. The χ^2 with ties (two degrees of freedom) was 16.96 (P=0.0002) Pairwise comparisons across groups was made with the Two-sample Wilcoxon rank-sum (Mann-Whitney) test.