- 1 Rapid and Adaptive Evolution of the Recombination Pathway in Mammals
- 2 Article

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8 Abstract

Meiotic recombination, the exchange of genetic material between homologous chromosomes during meiosis, is required for successful gametogenesis in most sexually reproducing species. Recombination is also a 10 fundamental evolutionary force, influencing the fate of new mutations and determining the genomic scale over 11 which selection shapes genetic variation. Despite the central importance of recombination, basic questions 12 about its evolution have yet to be addressed. Although many genes that play roles in recombination 13 have been identified, the molecular evolution of most of these genes remains uncharacterized. Using a 14 phylogenetic comparative approach, we measure rates of evolution in 32 recombination pathway genes across 16 mammalian species, spanning primates, murids, and laurasithians. By analyzing a carefully-selected panel of genes involved in key components of recombination – spanning double strand break formation, strand invasion, the crossover/non-crossover decision, and resolution – we generate a comprehensive picture of the 18 evolution of the recombination pathway in mammals. Recombination genes exhibit marked heterogeneity in the rate of protein evolution, both across and within genes. We report signatures of rapid evolution and positive selection that could underlie species differences in recombination rate.

- 22 Introduction
- 23 Results

- Table 1: Sequence divergence between Human (Homo sapiens) and Rhesus Macaque (Macaca mulatta)
- ²⁵ (Yang and Nielsen 2000, Yang (2007)). Steps: A double strand break (DSB) formation, B DSB processing
- & Strand Invasion, C Homologous Pairing, D1 crossover (CO) vs. non-crossover (NCO) step1 MutS, D2 -
- 27 CO vs. NCO step 2 MutL.

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Gene	bp	ω	S	N	t	κ	dN	dS	
A)									
SPO11	XXX	A	0.1434	291.2	896.8	0.0872	2.5317	0.0118 +/- 0.0036	0.0823 + / - 0.0178
MEI4	XXX	A	0.7252	331	824	0.0822	4.6295	0.0247 +/- 0.0056	0.0341 + / - 0.0104
REC114	XXX	A	0.3239	237.2	557.8	0.0974	2.9455	0.0200 +/- 0.0061	0.0618 +/- 0.0168

Table 2: PAML analysis of 32 recombination genes in mammals (Yang 2007).

Gene	bp	N	ω	M	M1-M2	$p ext{-}value$	M7-M8	$p ext{-}value$	M8a- $M8$	$p ext{-}value$
A)										
HORMAD1	1212	16	0.3036	7	0	1.000	1.795	0.4076	_	_
HORMAD2	981	15	0.3153	7	0	1.000	3.650	0.1612	_	_
MEI4	1170	16	0.4332	7	0	1.000	0.005	0.9976	_	_
REC114	870	15	0.4003	7	0	1.000	5.384	0.0677	_	_
IHO1	1824	16	0.7095	8	13.061	0.0015	17.571	0.0002	14.527	0.0001
SPO11	1188	15	0.1654	7	0	1.000	4.648	0.0980	_	_
В)										
MRE11	2136	16	0.1688	8	0.363	0.8342	11.931	0.0026	4.706	0.0301
NBS1	2289	15	0.4183	8	0	1.000	12.763	0.0017	4.087	0.0432
RAD50	3936	16	0.1006	7	0	1.000	0.301	0.8605		
BRCC3	954	15	0.0602	7	0	1.000	0.250	0.8826	_	_
DMC1	1020	15	0.0351	1	0.488	0.7835	5.000	0.0821	_	_
RAD51	1017	16	0.0268	7	0	1.000	0	1.000		_
SPATA22	1101	16	0.4893	7	0	1.000	0.429	0.8070	_	_
MEIOB	1425	16	0.2341	7	0	1.000	0.665	0.7172	_	_
MCMDC2	2052	16	0.2239	7	0	1.000	0.628	0.7307	_	_
C)										
REC8	1833	16	0.3698	8	0	1.000	14.690	0.0006	5.927	0.0149
RAD21L	1686	15	0.503	8	12.124	0.0023	32.050	>0.0001	12.049	0.0005
SYCP1	3015	16	0.4337	8	8.711	0.0128	26.860	>0.0001	9.243	0.0024
SYCP2	4650	16	0.5572	8	11.584	0.0031	37.200	>0.0001	15.838	0.0001
TEX12	369	14	0.2297	7	0.0565	0.9721	1.549	0.4610	_	_
D1)										
TEX11	2844	15	0.8483	8	60.872	>0.0001	82.665	>0.0001	61.141	>0.0001
SHOC1	4644	16	0.6113	8	12.447	0.0020	30.561	>0.0001	15.645	0.0001
CNTD1	1026	15	0.2496	7	0	1.000	0.936	0.6263	_	_
RNF212	948	16	0.5014	8	0	1.000	16.366	0.0003	5.202	0.0226
RNF212B	906	14	0.4066	7	0	1.000	0.500	0.7788	_	_
MSH4	2814	16	0.2132	8	16.608	0.0002	39.447	>0.0001	23.238	>0.0001

Gene	bp	N	ω	M	M1-M2	$p ext{-}value$	M7-M8	$p ext{-}value$	M8a-M8	$p ext{-}value$
MSH5	2565	15	0.1642	7	0	1.000	4.214	0.1216	_	_
D2)										
MER3	4458	16	0.3633	8a	0	1.000	12.838	0.0016	3.109	0.0779
HEI10	831	15	0.1226	7	0	1.000	0.250	0.8826	_	_
MLH1	2313	15	0.1652	8a	0	1.000	12.221	0.0022	0.280	0.5970
MLH3	4419	16	0.4444	7	0	1.000	3.757	0.1528	_	_
MUS81	1665	16	0.2124	7	0	1.000	0.628	0.7304	_	_

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