

Effect of Polymorphism on *IL1A* to Cancer Susceptibility: Evidence based on 34,016 subjects

Haoran Xia¹; Yiding Chen²; Jialin Meng^{1*}; Chaozhao Liang^{1*}

¹Department of Urology, the First Affiliated Hospital of Anhui Medical University; Institute of Urology and Anhui Province Key Laboratory of Genitourinary Diseases, Anhui Medical University, Hefei, Anhui, China.

²The First Clinical College of Anhui Medical University, Hefei, Anhui, China

Corresponding author:

Jialin Meng, MD, mengjialin@ahmu.edu.cn;

Chaozhao Liang, MD, PhD, liang_chaozhao@ahmu.edu.cn.

Running Title: Association between *IL1A* polymorphism and cancer susceptibility

rs3783553	Huang et al.	2016	*	*	*	*	*	*	*	*	NA
rs3783553	Pu et al.	2014	*	*	*	*	*	*	*	*	NA
rs3783553	Huang et al.	2015	*	*	*	*	*	*	*	*	NA
rs3783553	Yan et al.	2015	*	*	*	*	*	*	*	*	NA
rs3783553	Ma et al.	2018	*	*	*	*	*	*	*	*	NA
rs3783553	Yu et al.	2016	*	*	*	*	*	*	*	*	NA
rs3783553	Zeng et al.	2014	*	*	*	*	*	*	*	*	NA
rs3783553	Zhang et al.	2016	*	*	*	*	**	*	*	*	NA
rs3783553	Si et al.	2013	*	*	*	*	*	*	*	*	NA
rs3783553	Gao et al.	2009	*	*	*	*	*	*	*	*	NA
rs3783553	He et al.	2010	*	*	*	*	**	*	*	*	NA
rs3783553	Du et al.	2014	*	*	*	*	*	*	*	*	NA
rs3783553	Yang et al.	2012	*	*	*	*	*	*	*	*	NA
rs3783553	Zhang et al.	2015	*	*	*	*	*	*	*	*	NA
rs3783553	Zhang et al.	2014	*	*	*	*	*	*	*	*	NA
rs3783553	Liao et al.	2014	*	*	*	*	**	*	*	*	NA
rs3783553	Hashemi et al.	2017	*	*	*	*	*	*	*	*	NA
rs3783553	Gao et al.	2014	*	*	*	*	**	*	*	*	NA

This table identifies “high” quality choices with a “star”. A study can be awarded a maximum of 1 star for each numbered item within the Selection and Exposure categories. A

maximum of 2 stars can be given for Comparability. *, Yes; NA, not applicable. (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm).

Supplementary table 2. Details of the sensitivity analyses for *IL-1A* polymorphism and cancer risk.

SNP	Comparison	Study omitted	Estimate (95% Confident Interval)	Effect Model
rs17561	G vs. T	Bushley et al. (2004)	1.088904 (0.85087001-1.3935289)	Random
		Ai et al. (2014)	0.91306001 (0.73810124-1.1294909)	
		Zidi et al. (2015)	0.97022778 (0.70064855-1.3435296)	
		Sousa et al. (2016)	1.0545193 (0.75914383-1.4648224)	
		Eaton et al. (2018)	1.0078928 (0.67916292-1.4957353)	
		Combined	0.99916719 (0.77064547-1.2954531)	
	G/G vs. T/T	Bushley et al. (2004)	0.97866172 (0.70411134-1.3602662)	Fixed
		Ai et al. (2014)	0.95101762 (0.69111377-1.3086623)	
		Zidi et al. (2015)	0.88702357 (0.62424099-1.260428)	
		Sousa et al. (2016)	0.98404658 (0.69199985-1.3993467)	
		Eaton et al. (2018)	1.1361963 (0.72247756-1.7868264)	
		Combined	0.9709016 (0.70801326-1.3314015)	
	G/T vs. T/T	Bushley et al. (2004)	1.1823874 (0.80174726-1.7437413)	Random
		Ai et al. (2014)	0.87386686 (0.56693363-1.3469714)	
		Zidi et al. (2015)	0.93803257 (0.58291847-1.5094821)	
		Sousa et al. (2016)	1.1203972 (0.67112821-1.8704172)	
		Eaton et al. (2018)	0.9892149 (0.53651553-1.8238915)	
		Combined	1.012089 (0.664478-1.5415472)	
	G/G+G/T vs. T/T	Bushley et al. (2004)	1.1729126 (0.81055802-1.6972554)	Random
		Ai et al. (2014)	0.88139558 (0.60731953-1.2791588)	
Zidi et al. (2015)		0.95207816 (0.61710626-1.4688764)		
Sousa et al. (2016)		1.119821 (0.69166809-1.8130065)		
Eaton et al. (2018)		1.0164936 (0.57230759-1.8054265)		
Combined		1.019146 (0.69271149-1.4994102)		
G/G vs. G/T+ T/T	Bushley et al. (2004)	0.92898875 (0.69154781-1.2479544)	Fixed	
	Ai et al. (2014)	0.92099231 (0.69067943-1.2281049)		
	Zidi et al. (2015)	0.88969368 (0.63079309-1.2548566)		
	Sousa et al. (2016)	0.91457665 (0.67000544-1.2484233)		

rs1800587	C vs. T	Eaton et al. (2018)	1.0723299 (0.73254085-1.56973)	Random
		Combined	0.93546229 (0.70335961-1.2441569)	
		Foster et al. (2000)	1.1143869 (1.0124718-1.2265606)	
		Bushley et al. (2004)	1.1356614 (1.0361882-1.2446839)	
		Grimm et al. (2004)	1.110695 (1.0099071-1.2215414)	
		Hefler et al. (2005)	1.1254553 (1.020059-1.2417414)	
		Snoussi et al. (2005)	1.12156 (1.0162802-1.237746)	
		Wang et al. (2005)	1.102581 (1.0072669-1.2069144)	
		Wang et al. (2005)	1.1210726 (1.0190992-1.2332498)	
		Rothman et al. (2006)	1.1349921 (1.0174309-1.2661374)	
		Hou et al. (2007)	1.1343535 (1.0282907-1.2513561)	
		Abazis-Stamboulieh et al. (2007)	1.084224 (1.99868965-1.1770842)	
		Braicu et al. (2007)	1.1149794 (1.0125859-1.2277269)	
		Ennas et al. (2008)	1.1190773 (1.0172055-1.2311515)	
		Hoefl et al. (2008)	1.1333628 (1.0247077-1.2535391)	
		Saenz-Lopez et al. (2008)	1.1199923 (1.0146664-1.2362514)	
		Yang et al. (2011)	1.1125885 (1.0094941-1.2262114)	
		Senguven et al. (2011)	1.1242776 (1.0226165-1.2360452)	
		Eshghyar et al. (2012)	1.1219686 (1.0197638-1.2344168)	
		Zheng et al. (2013)	1.1366767 (1.0362171-1.2468756)	
Bai et al. (2013)	1.1196498 (1.0172349-1.2323757)			
Ai et al. (2014)	1.1168118 (1.0147569-1.2291304)			
Qu et al. (2014)	1.0822709 (0.9969182-1.1749312)			
Eaton et al. (2018)	1.1301898 (1.0213937-1.2505746)			
C/C vs. T/T	Combined	1.118608 (1.0191256-1.2278014)	Random	
	Foster et al. (2000)	1.2595074 (1.0276887-1.5436182)		
	Bushley et al. (2004)	1.2755945 (1.0422684-1.5611538)		
	Grimm et al. (2004)	1.207817 (1.0004098-1.4582243)		
	Hefler et al. (2005)	1.2581778 (1.0249351-1.544499)		
	Snoussi et al. (2005)	1.279283 (1.0352877-1.5807829)		
	Wang et al. (2005)	1.2133173 (1.0086539-1.4595082)		
	Wang et al. (2005)	1.2474529 (1.0234329-1.5205088)		
	Rothman et al. (2006)	1.3221509 (1.0517963-1.6619977)		

	Hou et al. (2007)	1.3049545 (1.0567685-1.611428)
	Abazis-Stamboulieh et al. (2007)	1.2503132 (1.0214759-1.530416)
	Braicu et al. (2007)	1.2533375 (1.0237054-1.5344794)
	Ennas et al. (2008)	1.2605125 (1.0308017-1.5414134)
	Hoefl et al. (2008)	1.3073854 (1.0581926-1.6152605)
	Saenz-Lopez et al. (2008)	1.2819759 (1.0394988-1.5810139)
	Yang et al. (2011)	1.2233027 (1.0030125-1.4919748)
	Senguven et al. (2011)	1.2731194 (1.0410211-1.5569646)
	Eshghyar et al. (2012)	1.2719406 (1.0407513-1.5544854)
	Zheng et al. (2013)	1.2750037 (1.0495565-1.5488775)
	Bai et al. (2013)	1.2711959 (1.0396665-1.5542856)
	Ai et al. (2014)	1.2557689 (1.0308528-1.5297582)
	Qu et al. (2014)	1.1116145 (0.9829067-1.2571759)
	Eaton et al. (2018)	1.3096586 (1.0616697-1.6155736)
	Combined	1.2587642 (1.0353232-1.5304278)
C/T vs. T/T	Foster et al. (2000)	1.0678779 (0.92527735-1.2324555)
	Bushley et al. (2004)	1.1065238 (0.96485114-1.2689986)
	Grimm et al. (2004)	1.0803351 (0.93551069-1.2475796)
	Hefler et al. (2005)	1.0890478 (0.94084334-1.2605978)
	Snoussi et al. (2005)	1.0740495 (0.92791545-1.2431976)
	Wang et al. (2005)	1.0674819 (0.92709303-1.2291296)
	Wang et al. (2005)	1.09299 (0.95106083-1.2560998)
	Rothman et al. (2006)	1.0855165 (0.91879839-1.2824858)
	Hou et al. (2007)	1.0934082 (0.94439042-1.2659398)
	Abazis-Stamboulieh et al. (2007)	1.0376447 (0.96850878-1.1117158)
	Braicu et al. (2007)	1.0710588 (0.927046-1.2374432)
	Ennas et al. (2008)	1.0788815 (0.93542194-1.2443424)
	Hoefl et al. (2008)	1.0850056 (0.93175077-1.2634679)
	Saenz-Lopez et al. (2008)	1.066648 (0.92144102-1.2347376)
	Yang et al. (2011)	1.0781385 (0.93045139-1.2492673)
	Senguven et al. (2011)	1.085232 (0.9422909-1.2498565)
	Eshghyar et al. (2012)	1.0706885 (0.92975307-1.2329875)
	Zheng et al. (2013)	1.0984194 (0.95187145-1.2675295)

Random

	Bai et al. (2013)	1.0804635 (0.93844903-1.243969)	
	Ai et al. (2014)	1.0737259 (0.92910343-1.2408601)	
	Qu et al. (2014)	1.087394 (0.94156331-1.2558111)	
	Eaton et al. (2018)	1.075537 (0.92427945-1.2515476)	
	Combined	1.0772699 (0.937327-1.2381063)	
C/C+C/T vs. T/T	Foster et al. (2000)	1.1087502 (0.97873694-1.2560341)	Random
	Bushley et al. (2004)	1.1421711 (1.0150313-1.285236)	
	Grimm et al. (2004)	1.1145502 (0.98333162-1.2632791)	
	Hefler et al. (2005)	1.1279305 (0.99280584-1.2814461)	
	Snoussi et al. (2005)	1.1159658 (0.98217493-1.2679816)	
	Wang et al. (2005)	1.102262 (0.97713524-1.2434117)	
	Wang et al. (2005)	1.1265415 (0.99629366-1.2738171)	
	Rothman et al. (2006)	1.1318791 (0.97984719-1.3075001)	
	Hou et al. (2007)	1.1356647 (0.99991554-1.2898432)	
	Abazis-Stamboulieh et al. (2007)	1.0579948 (0.98488176-1.1365354)	
	Braicu et al. (2007)	1.1108475 (0.97981197-1.2594072)	
	Ennas et al. (2008)	1.1179013 (0.98710209-1.2660325)	
	Hoefl et al. (2008)	1.1305389 (0.99052262-1.2903475)	
	Saenz-Lopez et al. (2008)	1.1106211 (0.9773159-1.2621089)	
	Yang et al. (2011)	1.1140044 (0.9801383-1.2661536)	
	Senguven et al. (2011)	1.1241978 (0.99386185-1.2716262)	
	Eshghyar et al. (2012)	1.1134372 (0.98430306-1.2595128)	
	Zheng et al. (2013)	1.1405461 (1.0091571-1.2890415)	
	Bai et al. (2013)	1.1189629 (0.98937845-1.2655197)	
	Ai et al. (2014)	1.1142436 (0.98256022-1.2635754)	
	Qu et al. (2014)	1.1004988 (0.97278184-1.2449837)	
	Eaton et al. (2018)	1.1225507 (0.98330122-1.28152)	
	Combined	1.1165795 (0.98906238-1.260537)	
C/C vs. C/T+ T/T	Foster et al. (2000)	1.1986217 (0.98798895-1.4541602)	Random
	Bushley et al. (2004)	1.2037904 (0.99371541-1.4582763)	
	Grimm et al. (2004)	1.1459252 (0.95960277-1.368425)	

	Hefler et al. (2005)	1.1863148 (0.97797585-1.4390365)	
	Snoussi et al. (2005)	1.2143855 (0.99343115-1.4844834)	
	Wang et al. (2005)	1.1631856 (0.97187299-1.3921579)	
	Wang et al. (2005)	1.1742742 (0.97655863-1.4120195)	
	Rothman et al. (2006)	1.2445769 (1.0015415-1.5465877)	
	Hou et al. (2007)	1.2249411 (1.0011896-1.498698)	
	Abazis-Stamboulieh et al. (2007)	1.2185016 (1.0058209-1.4761535)	
	Braicu et al. (2007)	1.1920352 (0.98340696-1.4449238)	
	Ennas et al. (2008)	1.1945547 (0.98720819-1.4454507)	
	Hoefl et al. (2008)	1.2317958 (1.0079629-1.5053339)	
	Saenz-Lopez et al. (2008)	1.2186185 (0.99978876-1.4853448)	
	Yang et al. (2011)	1.1625154 (0.96313792-1.4031657)	
	Senguven et al. (2011)	1.2034172 (0.99400353-1.4569494)	
	Eshghyar et al. (2012)	1.2116463 (1.0032412-1.4633439)	
	Zheng et al. (2013)	1.209098 (1.0041413-1.4558887)	
	Bai et al. (2013)	1.2054635 (0.98818278-1.4705199)	
	Ai et al. (2014)	1.1920215 (0.98835331-1.4376593)	
	Qu et al. (2014)	1.0730265 (0.95573616-1.2047111)	
	Eaton et al. (2018)	1.2377387 (1.015813-1.5081488)	
	Combined	1.1949698 (0.99245048-1.4388153)	
rs3783553	Gao et al. (2009)	1.3071965 (1.2001635-1.423775)	Random
	He et al. (2010)	1.2850665 (1.1898788-1.3878689)	
	Yang et al. (2012)	1.2926877 (1.1950018-1.3983588)	
	Si et al. (2013)	1.2943312 (1.1970245-1.3995479)	
	Pu et al. (2014)	1.2935164 (1.194968-1.4001921)	
	Zeng et al. (2014)	1.3019085 (1.2022203-1.4098628)	
	Du et al. (2014)	1.3255397 (1.2407275-1.4161493)	
	Zhang et al. (2014)	1.2959334 (1.197322-1.4026664)	
	Liao et al. (2014)	1.2835401 (1.1915337-1.382651)	
	Gao et al. (2014)	1.3187627 (1.2234336-1.4215196)	
	Huang et al. (2015)	1.3165137 (1.2205408-1.420033)	
	Yan et al. (2015)	1.3104022 (1.2105973-1.4184353)	
	Zhang et al. (2015)	1.2890154 (1.1923161-1.3935574)	

Ins/Ins vs. Del/Del	Huang et al. (2016)	1.2977227 (1.1988615-1.4047363)	Random
	Yu et al. (2016)	1.3042229 (1.2042254-1.4125242)	
	Zhang et al. (2016)	1.2984432 (1.1974051-1.408007)	
	Hashemi et al. (2017)	1.2925507 (1.1962954-1.3965509)	
	Ma et al. (2018)	1.2884655 (1.1916558-1.3931401)	
	Combined	1.2995767 (1.204766-1.4018487)	
	Gao et al. (2009)	1.9219596 (1.5846775-2.3310289)	
	He et al. (2010)	1.8110595 (1.5312898-2.1419435)	
	Yang et al. (2012)	1.8697686 (1.5612833-2.2392058)	
	Si et al. (2013)	1.8636128 (1.5615518-2.2241035)	
	Pu et al. (2014)	1.866032 (1.558496-2.2342539)	
	Zeng et al. (2014)	1.8732952 (1.5661392-2.2406914)	
	Du et al. (2014)	1.9484318 (1.7017984-2.2308087)	
	Zhang et al. (2014)	1.8809477 (1.5698572-2.2536855)	
	Liao et al. (2014)	1.8444762 (1.5523897-2.1915197)	
	Gao et al. (2014)	1.9416754 (1.637585-2.3022339)	
	Huang et al. (2015)	1.892611 (1.5823245-2.2637432)	
	Yan et al. (2015)	1.9162278 (1.5995845-2.2955518)	
	Zhang et al. (2015)	1.8607125 (1.5545005-2.2272434)	
	Huang et al. (2016)	1.8711363 (1.563525-2.2392678)	
Yu et al. (2016)	1.8911828 (1.5776503-2.2670248)		
Zhang et al. (2016)	1.8751723 (1.5610883-2.2524486)		
Hashemi et al. (2017)	1.8552758 (1.5592065-2.2075641)		
Ma et al. (2018)	1.829358 (1.5380909-2.175782)		
Combined	1.8785419 (1.5822952-2.2302536)		
Ins/Del vs. Del/Del	Gao et al. (2009)	1.5071969 (1.3368073-1.6993043)	Fixed
	He et al. (2010)	1.4273287 (1.2803806-1.5911419)	
	Yang et al. (2012)	1.4509373 (1.3016137-1.6173916)	
	Si et al. (2013)	1.4511584 (1.3033201-1.6157665)	
	Pu et al. (2014)	1.4504504 (1.3010137-1.6170517)	
	Zeng et al. (2014)	1.4448718 (1.2970369-1.6095568)	

	Du et al. (2014)	1.5526042 (1.3845553-1.7410499)		
	Zhang et al. (2014)	1.458493 (1.308733-1.6253903)		
	Liao et al. (2014)	1.4535096 (1.3057805-1.6179518)		
	Gao et al. (2014)	1.4798752 (1.3272656-1.6500318)		
	Huang et al. (2015)	1.4393282 (1.2923839-1.6029801)		
	Yan et al. (2015)	1.4604594 (1.3097242-1.6285424)		
	Zhang et al. (2015)	1.4541605 (1.3038584-1.6217885)		
	Huang et al. (2016)	1.4442477 (1.2960093-1.6094418)		
	Yu et al. (2016)	1.4493176 (1.3003861-1.6153059)		
	Zhang et al. (2016)	1.4439144 (1.2932109-1.61218)		
	Hashemi et al. (2017)	1.4581063 (1.3073338-1.6262671)		
	Ma et al. (2018)	1.4252414 (1.2779493-1.5895098)		
	Combined	1.457143 (1.31018-1.6205909)		
Ins/Ins+Ins/Del vs. Del/Del	Gao et al. (2009)	1.6985122 (1.4551148-1.9826225)	Random	
	He et al. (2010)	1.6059269 (1.4035263-1.8375154)		
	Yang et al. (2012)	1.6540114 (1.4286557-1.9149144)		
	Si et al. (2013)	1.6507349 (1.429889-1.9056903)		
	Pu et al. (2014)	1.652419 (1.4274924-1.9127868)		
	Zeng et al. (2014)	1.6497352 (1.4278957-1.90604)		
	Du et al. (2014)	1.6964006 (1.5200669-1.8931899)		
	Zhang et al. (2014)	1.6645967 (1.4371669-1.9280169)		
	Liao et al. (2014)	1.6459349 (1.428091-1.897009)		
	Gao et al. (2014)	1.6977249 (1.4773299-1.9509996)		
	Huang et al. (2015)	1.6505743 (1.4292976-1.9061083)		
	Yan et al. (2015)	1.6810606 (1.4507186-1.9479758)		
	Zhang et al. (2015)	1.6548196 (1.4282278-1.9173609)		
	Huang et al. (2016)	1.648574 (1.4259542-1.9059492)		
	Yu et al. (2016)	1.6615536 (1.4346309-1.9243699)		
	Zhang et al. (2016)	1.6537962 (1.4256699-1.9184257)		
	Hashemi et al. (2017)	1.6695222 (1.4395225-1.93627)		
	Ma et al. (2018)	1.6118275 (1.4046525-1.8495591)		
		Combined	1.6588842 (1.4430901-1.9069473)	

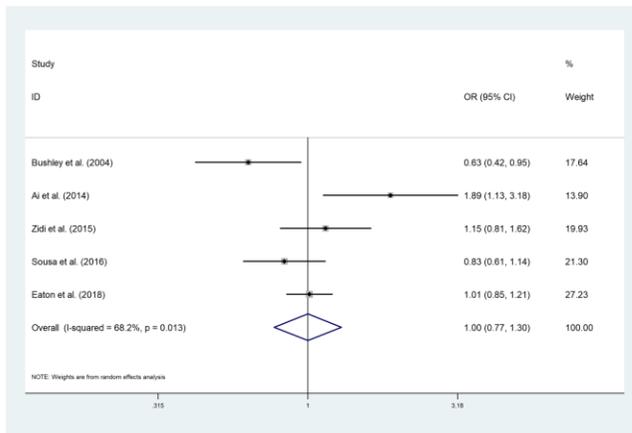
Ins/Ins vs.
Ins/Del+
Del/Del

Gao et al. (2009)	1.3106894 (1.1735069-1.4639087)
He et al. (2010)	1.2913545 (1.1672875-1.4286082)
Yang et al. (2012)	1.3001746 (1.1738534-1.4400895)
Si et al. (2013)	1.3012369 (1.1757085-1.4401675)
Pu et al. (2014)	1.2987543 (1.1719007-1.4393394)
Zeng et al. (2014)	1.3138226 (1.1850055-1.4566427)
Du et al. (2014)	1.3382947 (1.2168105-1.4719077)
Zhang et al. (2014)	1.3010944 (1.1744685-1.4413726)
Liao et al. (2014)	1.2828965 (1.1679553-1.4091494)
Gao et al. (2014)	1.3300513 (1.2050521-1.4680166)
Huang et al. (2015)	1.33363 (1.2183076-1.4598686)
Yan et al. (2015)	1.3221723 (1.1936905-1.4644831)
Zhang et al. (2015)	1.291052 (1.1680293-1.4270321)
Huang et al. (2016)	1.3089856 (1.1810867-1.4507346)
Yu et al. (2016)	1.316718 (1.1878179-1.4596061)
Zhang et al. (2016)	1.3067567 (1.1762164-1.4517848)
Hashemi et al. (2017)	1.2982341 (1.1782374-1.4304519)
Ma et al. (2018)	1.3002537 (1.1725186-1.4419044)
Combined	1.3078887 (1.1857435-1.4426163)

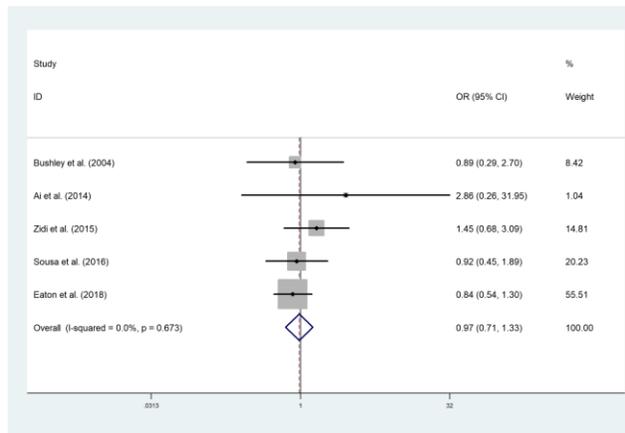
Random

Supplementary table 3. *P* values of the Egger's test for *IL-1A* polymorphism.

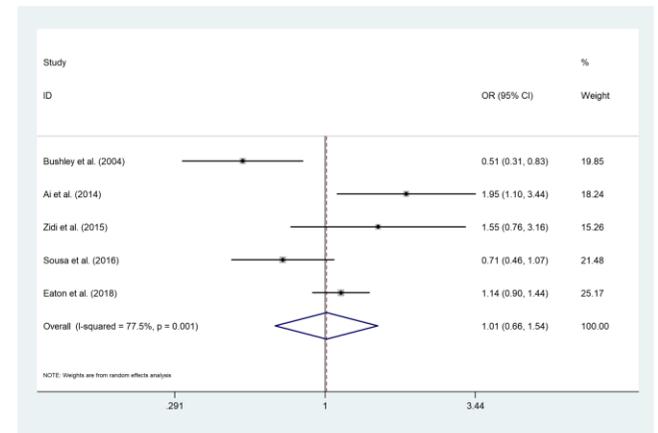
Polymorphisms	Subgroup	Egger's test $P > t $
rs17561	Overall	0.855
	HB	0.669
rs1800587	Overall	0.139
	Asians	0.829
	Caucasians	0.108
	PB	0.155
	HB	0.75
	Y	0.319
rs3783553	N	0.599
	Overall	0.079
	Asian	0.147
	PB	0.117
	HCC	0.747



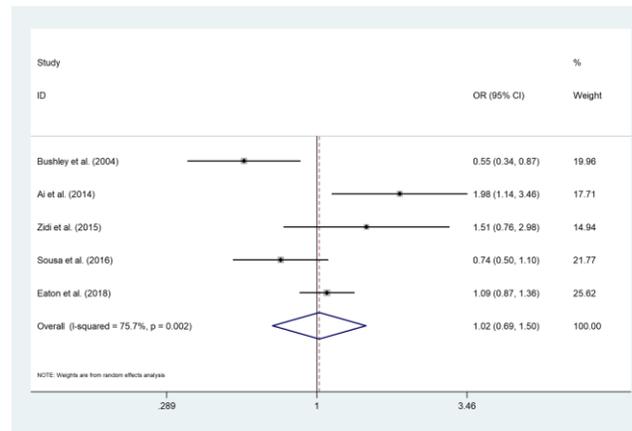
B vs. A



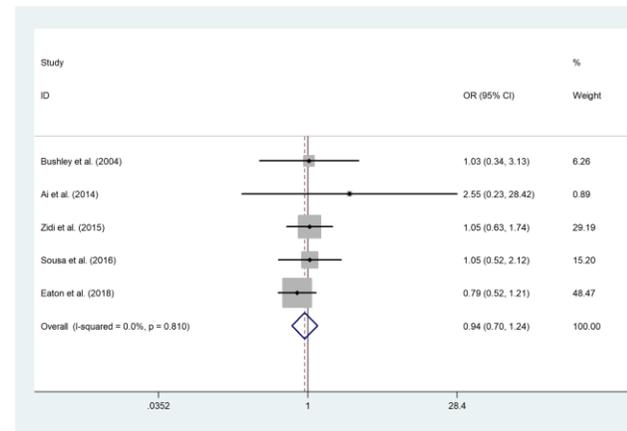
BB vs. AA



BA vs. AA



BB+BA vs. AA



BB vs. BA+AA

Fig.S1 Meta-analysis of the association between IL-1A rs17561 polymorphism and cancer risk.