The University of Hong Kong
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記者招待會

2018年4月26日

Speakers 講者

香港大學愛滋病研究所成功研發用於愛滋病預防和免疫治療的創新型廣譜抗體藥物

HKU Invents Universal Antibody Drug for HIV-1 Prevention and Immunotherapy

Professor CHEN Zhiwei 陳志偉教授

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AIDS 愛滋病研究所 Institute

此項研究發表在四月份《臨床研究雜誌》

The new findings are published in the April issue of *Journal of Clinical Investigation*.

JCI The Journal of Clinical Investigation

Tandem bispecific neutralizing antibody eliminates HIV-1 infection in humanized mice

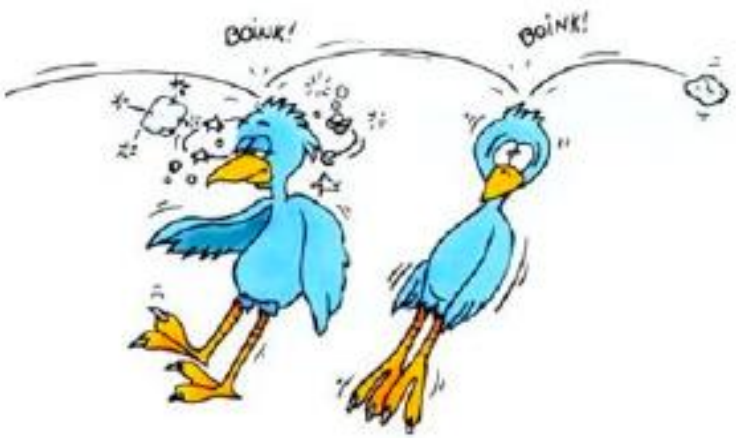
Xilin Wu, Jia Guo, Mengyue Niu, Minghui An, Li Liu, Hui Wang, Xia Jin, Qi Zhang, Ka Shing Lam, Tongjin Wu, Hua Wang, Qian Wang, Yanhua Du, Jingjing Li, Lin Cheng, Hang Ying Tang, Hong Shang, Linqi Zhang, Paul Zhou, **Zhiwei Chen**

J Clin Invest. https://doi.org/10.1172/JCI96764.

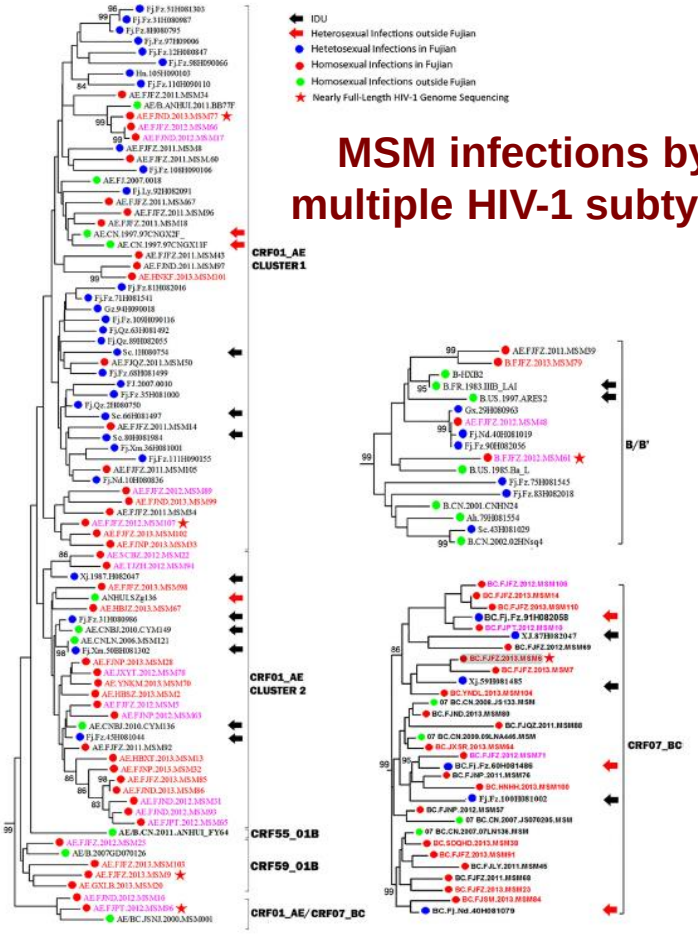
多亞型愛滋病病毒在中國平行傳播的現狀

HIV-1 is a genetically diverse pathogen：co-spreading of multiple subtypes in Hong Kong and mainland China

Kill two birds with one stone

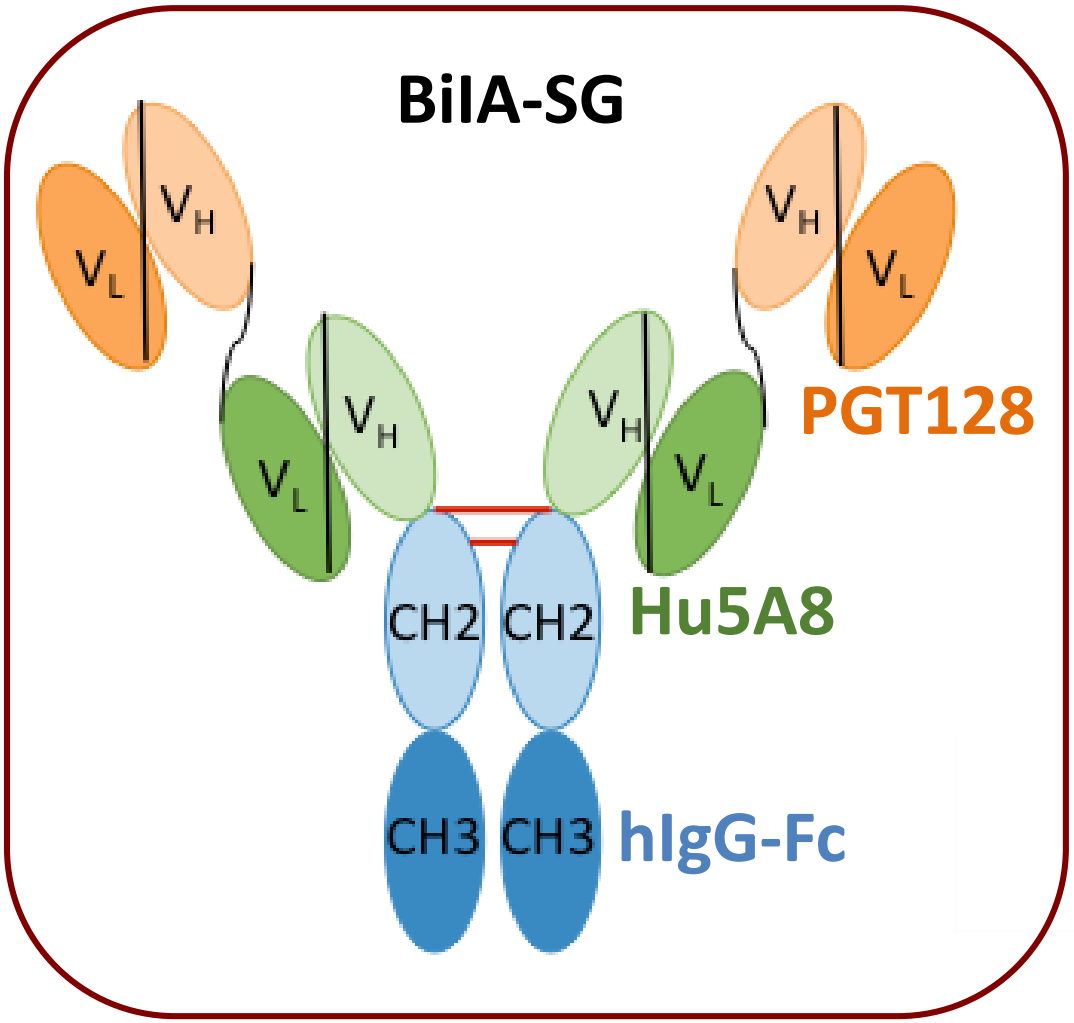


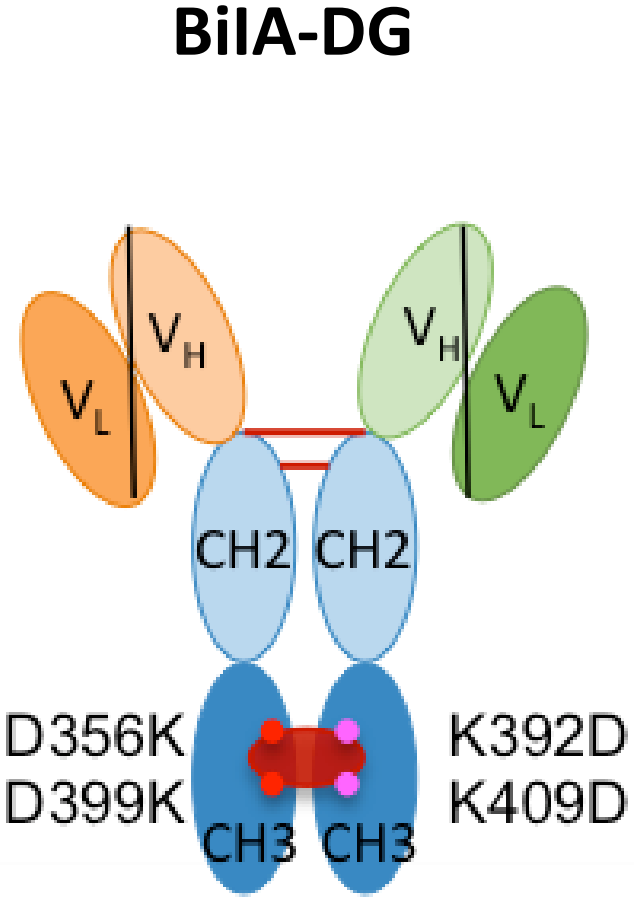
MSM infections by multiple HIV-1 subtypes



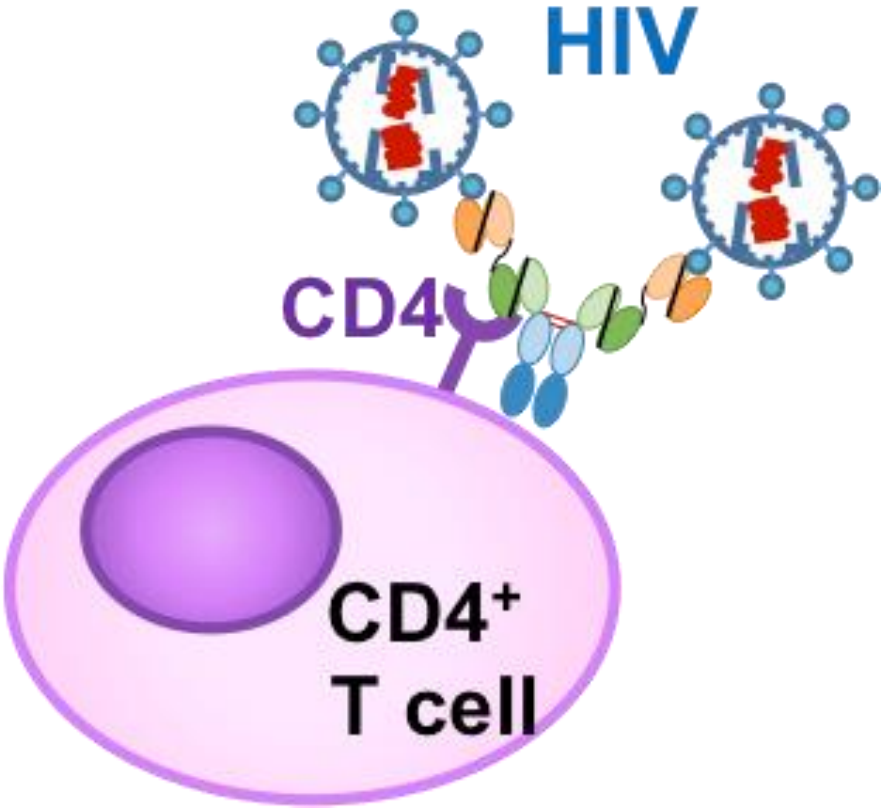
Chen et al. J Med Virol. 2018 Mar 25.
doi: 10.1002/jmv.25072. [Epub ahead of print]

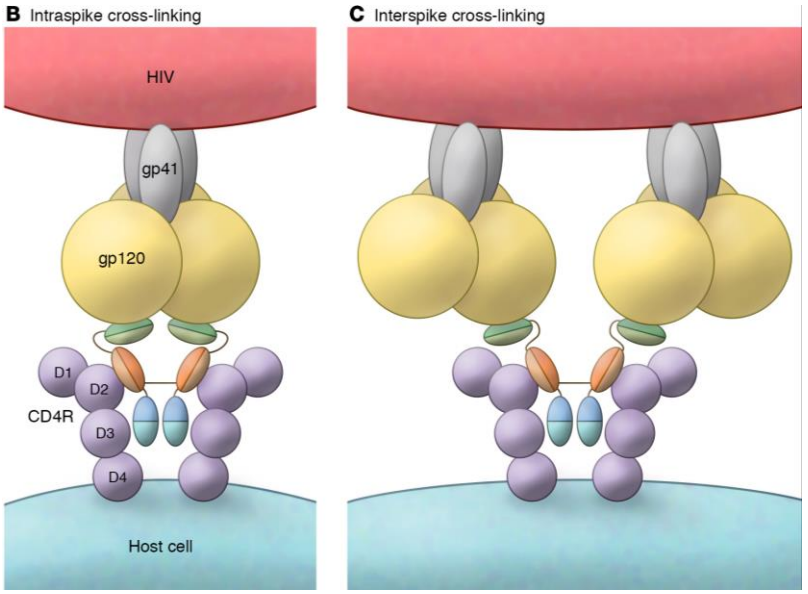
創新型串聯雙價中和抗體的設計
Design of a novel tandem bispecific neutralizing antibody





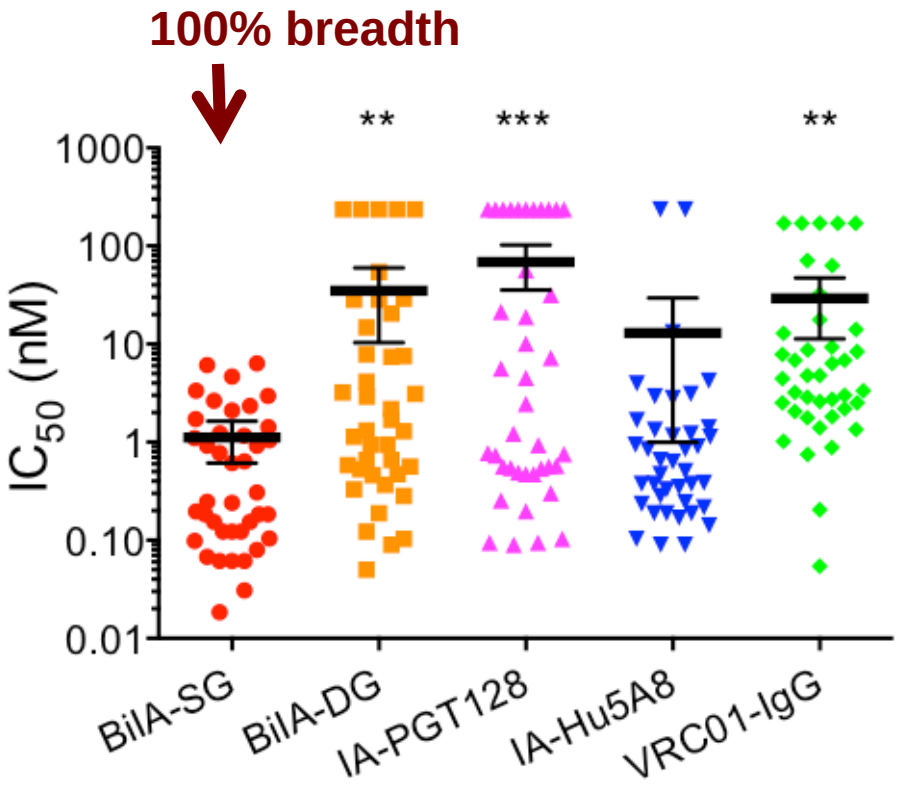
創新型串聯雙價中和抗體的工作原理
Possible mode of BiIA-SG action

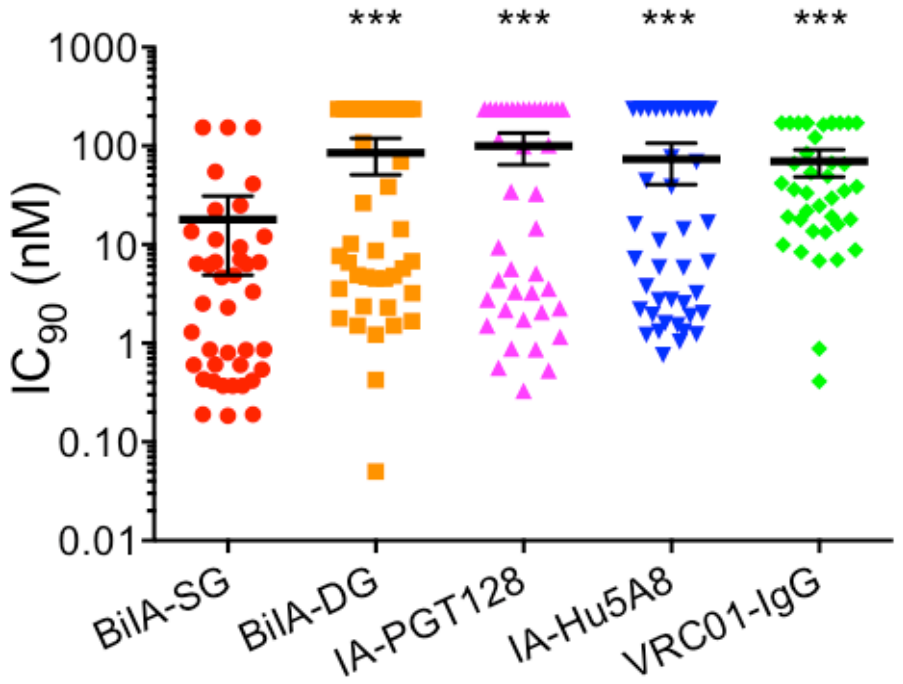




J Clin Invest. https://doi.org/10.1172/JCI121078.

串聯雙價中和抗體抗愛滋病毒的能力
Anti-HIV potency and breadth of BiIA-SG





串聯雙價中和抗體與單價廣譜中和抗體的比較

Comparison of neutralizing activity between BiIA-SG and bnAbs against 8 acute HIV-1 pseudoviruses

Virus			IC_{50}							
			V3-CD4	CD4bs		V2 glycan		V3 glycan		gp41
Subtype	Strain	Stage	BiIA-SG	VRC01	3BNC117	PG09	PG16	10-1074	PGT121	10E8
CRF01_AE	MG03	Acute	0.0323	/	2.4380	0.1056	/	/	/	2.5190
	P08	Acute	0.0032	/	1.0760	0.7809	/	/	/	/
B	MG01	Acute	0.0143	0.1906	0.0490	/	/	0.1680	0.0234	/
	TRO.11	Acute	0.0962	0.2162	0.0772	0.1659	1.1630	0.1598	0.0519	/
C	CE1176	Fiebig I/II	0.0095	1.3740	0.5785	0.0078	0.0093	0.0406	0.0340	0.9486
	25710	Fiebig V	0.0102	0.8191	0.1118	0.0245	0.0189	0.1370	0.0265	0.4062
CRF07_BC	MG17	Acute	0.0060	0.1512	0.1151	0.2911	0.1020	0.0457	0.0466	0.0140
	BJOX19	Acute	0.0138	0.9807	0.5602	0.1088	0.0812	0.0928	0.0240	1.2310
Virus			IC_{90}							
			V3-sCD4	CD4bs		V2 glycan		V3 glycan		gp41
Subtype	Strain	Stage	BiIA-SG	VRC01	3BNC117	PG09	PG16	10-1074	PGT121	10E8
CRF01_AE	MG03	Acute	0.1101	/	/	0.6671	/	/	/	/
	P08	Acute	0.0330	/	2.2966	/	/	/	/	/
B	MG01	Acute	0.0646	0.9623	0.7253	/	/	1.4242	0.2832	/
	TRO.11	Acute	0.4571	/	1.1814	/	/	1.5258	0.5185	/
C	CE1176	Fiebig I/II	0.0299	/	/	0.0389	0.0364	0.1300	0.1168	/
	25710	Fiebig V	0.0215	/	1.7800	0.4760	0.0408	1.1885	0.1157	/
CRF07_BC	MG17	Acute	0.0288	3.2295	0.2985	0.3179	0.3763	/	0.1791	/
	BJOX19	Acute	0.1130	/	/	1.2422	0.1515	0.2858	0.1125	/

(μg/ml)

- < 0.01
- 0.01-0.1
- 0.1-1.0
- 1.0-3.5
- > 3.5

*Unk: Unknown

串聯雙價中和抗體抗愛滋病毒的廣譜性能

Universal neutralizing activity against all HIV-1 strains tested

Virus			IC50		IC90	
			V3-CD4	CD4bs	V3-CD4	CD4bs
Subtype	Name	Stage	BiIA-SC	VRC01	BiIA-SC	VRC01
A	398F1	Unk*	0.0053	0.1841	0.0064	2.669
AC	246F3	Fiebig VI	0.0022	0.1253	0.0075	1.5178
CRF01_AE	CNE8	Chronic	0.007	1.09	0.068	/
	CNE55	Chronic	0.0385	0.2765	0.2371	2.983
	CNE3	Chronic	0.0487	2.9175	0.1166	/
	CNE5	Chronic	0.0208	0.1942	0.0774	/
	CNE59	Chronic	0.1968	0.7721	0.2316	/
	CNE107	Chronic	0.1413	1.245	0.3104	/
	MG03(BJOX5)	Fiebig VII	0.0395	2.0465	0.2078	/
	BJOX09	Fiebig IV	0.0001	1.4855	0.0006	/
	MG07(BJOX10)	Fiebig VII	0.0008	/	0.0059	/
	BJOX15	Fiebig VII	0.0441	0.5041	0.0832	/
	BJOX17	Fiebig VI	0.0002	/	0.0014	/
	MG10(BJOX18)	Fiebig IV	0.0212	/	0.1049	/
	MG11(BJOX21)	Fiebig VI	<0.0001	/	<0.0001	/
	BJOX23	Fiebig IV	0.0006	1.1605	0.0036	/
	MG15.33(BJOX25.01)	Fiebig VII	0.0656	1.983	0.2955	/
	MG15.36(BJOX25.05)	Fiebig VII	0.0253	2.8457	0.2092	/
	MG18(BJOX28.10)	Fiebig VII	0.0005	0.1195	0.0041	1.0648
	BJOX28.34	Fiebig VII	0.0565	0.1606	0.0993	1.394
	BJOX28.43	Fiebig VII	0.0162	0.494	0.0278	/
	BJOX31	Fiebig V	0.0606	0.9298	0.073	/
	P08	Fiebig IV	0.0422	1.736	0.1018	/
	P11	Fiebig IV	0.055	3.131	0.1443	/
B	TRO11	Fiebig III	0.0088	0.4943	0.0435	/
	X2278	Fiebig V/VI	0.0059	0.1691	0.0295	0.4082
	MG01(BJOX3)	Fiebig VII	0.0466	0.1124	0.125	0.9256
	MG02(BJOX4)	Fiebig VI	0.0045	3.08	0.0966	/
	MG08(BJOX6)	Fiebig IV	0.0607	0.689	0.1241	/
	MG04(BJOX7)	Fiebig V	<0.0001	0.1907	<0.0001	1.8137
	BJOX14	Fiebig V	<0.0001	0.7657	<0.0001	/
	MG09(BJOX20)	Fiebig VII	0.0486	2.0815	0.1079	/
	MG13(BJOX22)	Fiebig IV	0.1903	0.3645	0.2479	3.037
	MG23(BJOX41)	Fiebig V	0.0104	/	0.0392	/
	BJOX46	Fiebig V	<0.0001	0.547	0.0004	/
	JR-FL	Chronic	0.0426	0.0145	0.2635	0.1951
	SF162	Chronic	0.1728	0.0848	0.1919	1.1685

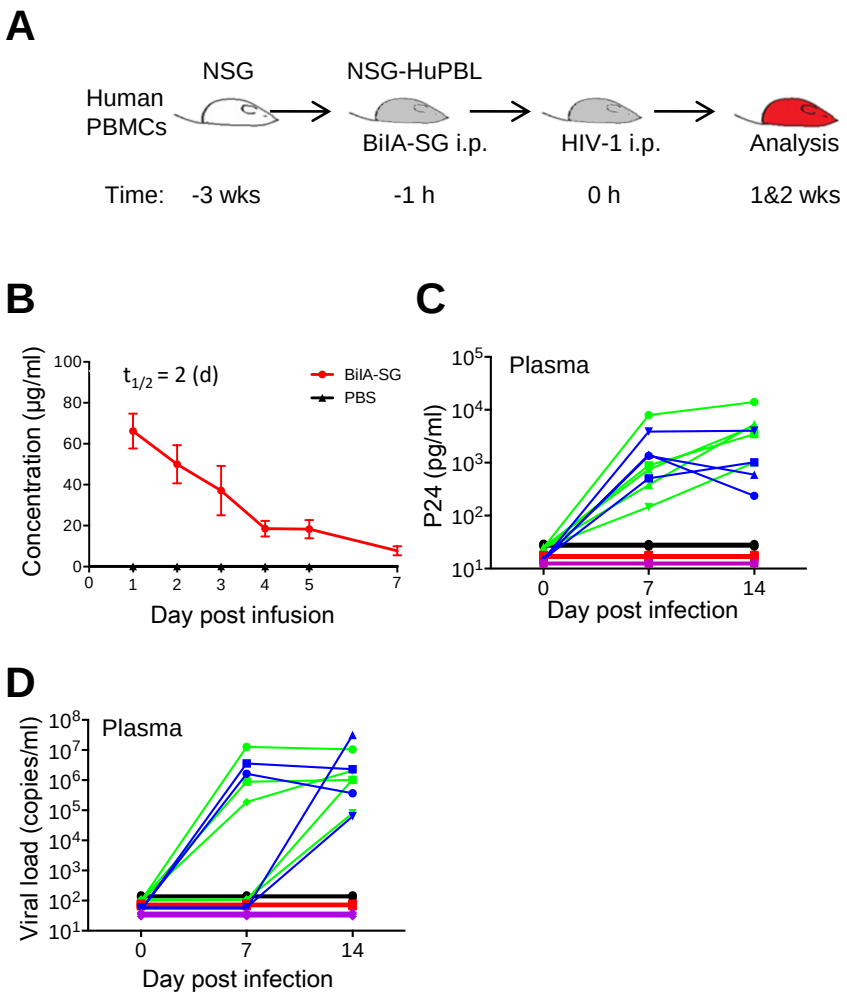
Virus			IC80		IC90	
			V3-CD4	CD4bs	V3-CD4	CD4bs
Subtype	Name	Stage	BiIA-SC	VRC01	BiIA-SC	VRC01
B'	CNE1	Chronic	0.0316	0.0101	0.1674	0.0649
	CNE4	Chronic	0.0464	1.289	0.4121	/
	CNE6	Chronic	0.0435	/	0.0933	/
	CNE9	Chronic	<0.0001	/	0.0009	/
	CNE10	Chronic	0.0413	1.0622	0.0722	/
	CNE11	Chronic	0.052	0.5238	0.0722	/
	CNE14	Chronic	0.0521	0.3581	0.3916	/
	CNE57	Chronic	0.0485	0.9678	0.2543	/
CRF07_BC	CNE19	Chronic	0.0915	0.1862	0.45	/
	CNE20	Chronic	0.0219	1.206	0.0306	/
	CNE21	Chronic	0.3707	0.2493	0.3706	/
	CNE40	Chronic	0.5708	0.5761	0.5525	/
	CNE68	Chronic	0.1888	0.6502	0.2233	/
	CNE23	Chronic	0.0314	/	0.1217	/
	CNE30	Chronic	<0.0001	1.1075	0.0004	/
	CNE46	Chronic	0.0511	0.8708	0.2963	/
	CNE47	Chronic	<0.0001	/	<0.0001	/
	CNE49	Chronic	0.0538	0.1397	0.3491	/
	CNE53	Chronic	0.0183	0.0174	0.0327	1.9306
	BJOX11	Fiebig V	0.003	0.365	0.0155	/
	BJOX16	Fiebig VI	0.0661	0.2937	0.0752	2.695
	BJOX19	Fiebig VII	0.003	1.496	0.0127	/
	M14(BJOX27)	Fiebig V	<0.0001	0.1738	<0.0001	1.3745
	MG17(BJOX29)	Fiebig V	0.0015	0.4458	0.0059	/
	BJOX37	Fiebig V	<0.0001	2.2275	0.0002	/
	CH119	Chronic	0.0115	0.2741	0.0919	/
	BJOX2000	Fiebig VII	0.0172	/	0.1034	/
C	CNE2	Chronic	0.022	0.2513	0.0313	3.4345
	CNE17	Chronic	0.0412	1.2144	0.2978	/
	CNE58	Chronic	0.1218	0.0262	0.7748	1.8234
	CNE65	Chronic	<0.0001	1.8585	0.0001	/
	CE0217	Fiebig V/VI	0.0177	0.1058	0.0721	0.2857
	CE1176	Fiebig VII	0.0095	1.248	0.0299	/
	25710	Fiebig V	0.0102	0.5594	0.0215	0.8704
G	X1632	Chronic	0.0835	0.1063	0.3242	0.2197

(μg/ml)
<0.001
0.01–0.1
0.1 – 1
1 – 3.5
/ > 3.5

*Unk: Unknown

BiIA-SG保護人源化小鼠免於多種HIV-1感染

BiIA-SG confers sterile protection against genetically divergent HIV-1 challenges in humanized mice



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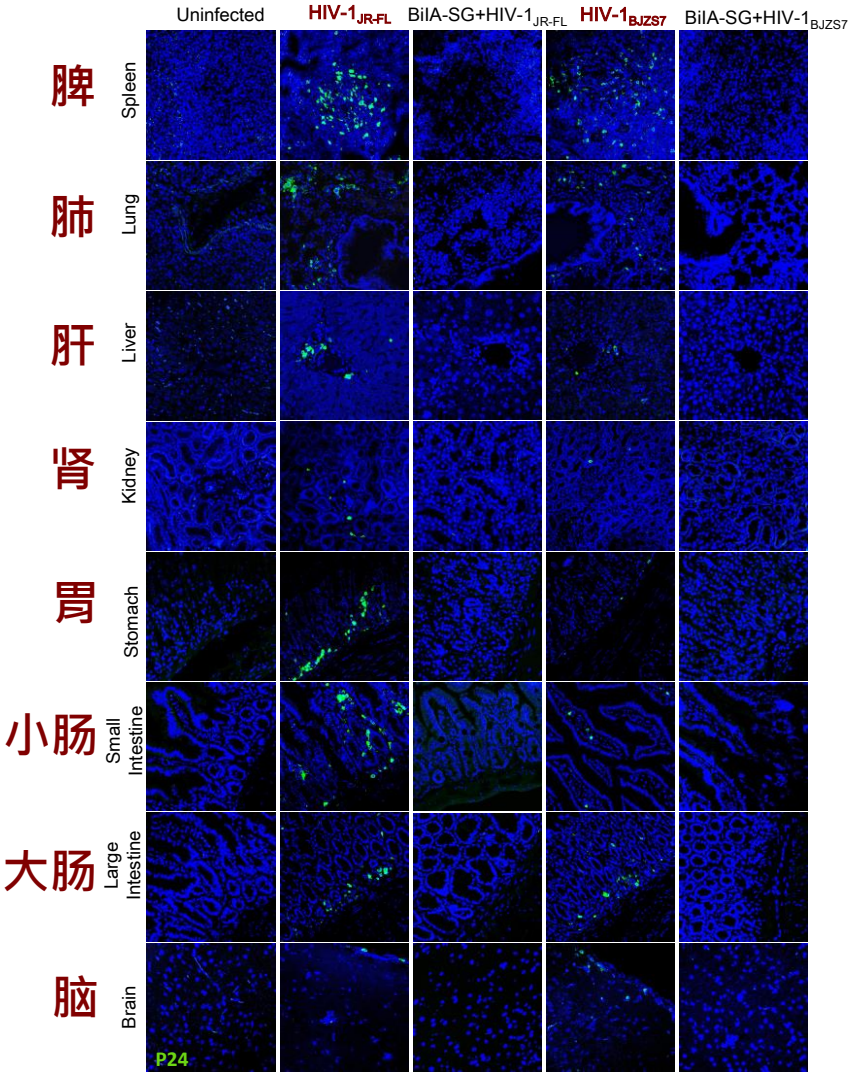
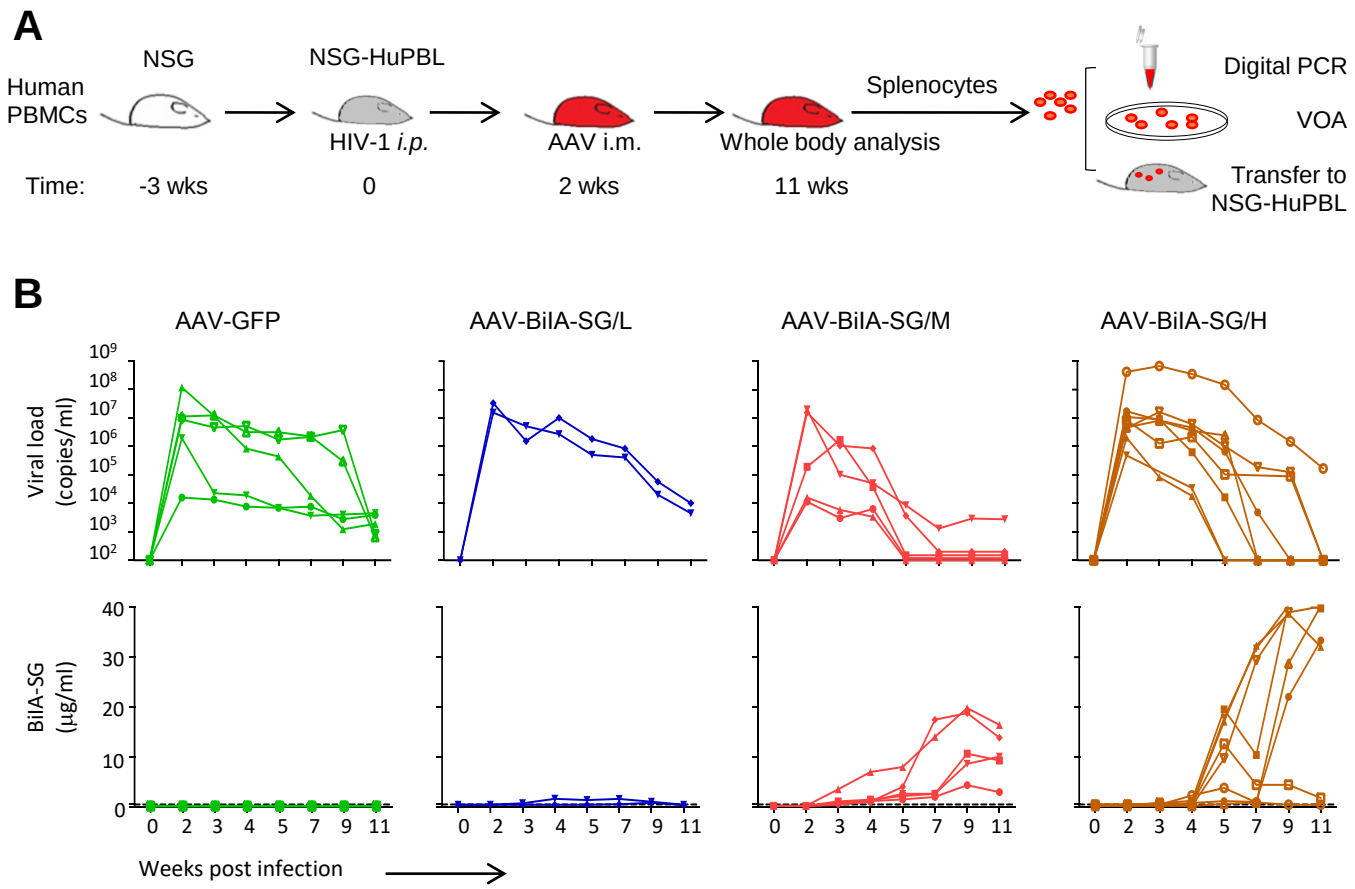


基因導入BiIA-SG可有效清除人源化小鼠體內受HIV感染的細胞

Single injection of AAV-vectored BiIA-SG eliminates HIV-infected splenocytes in humanized mice



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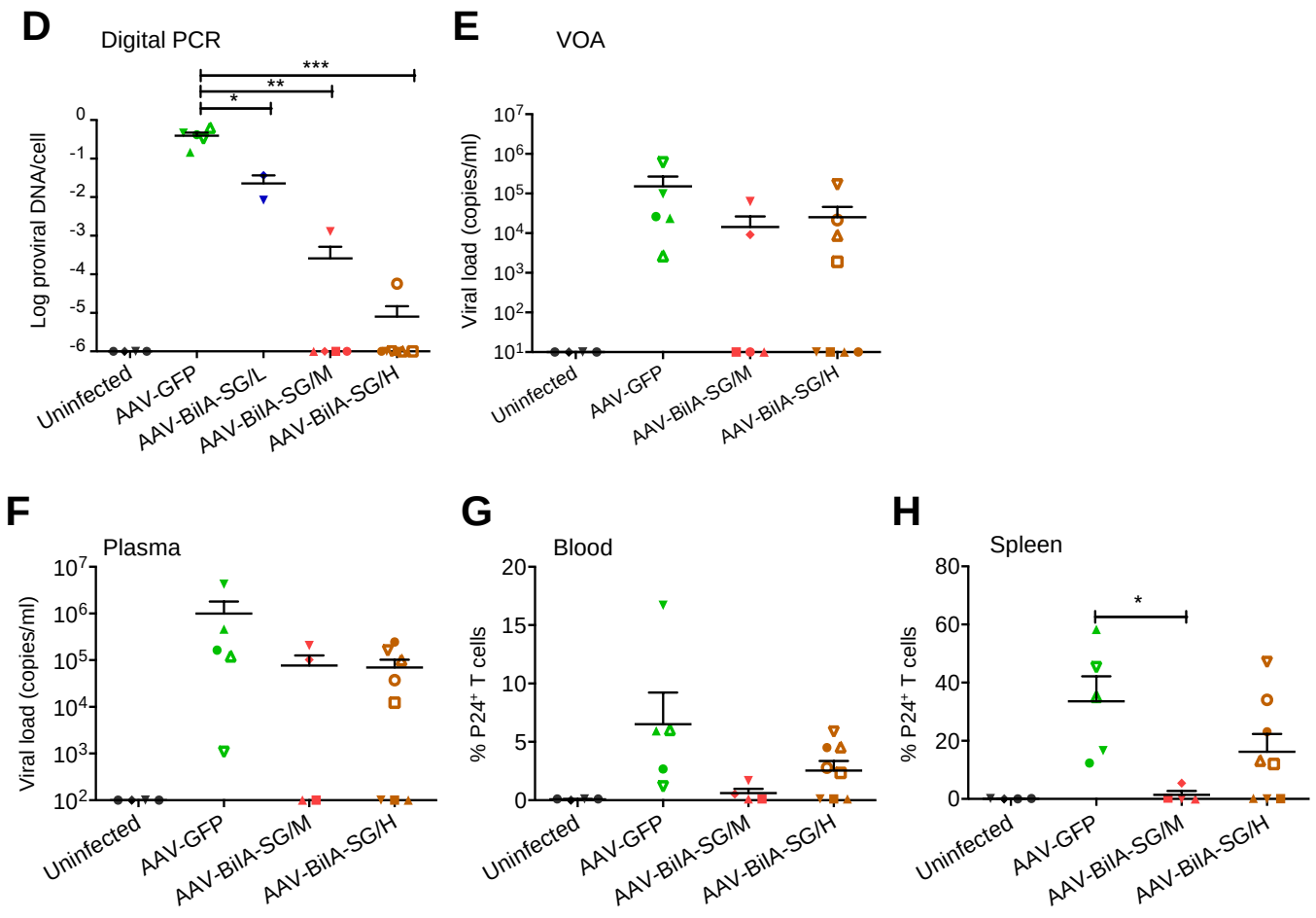

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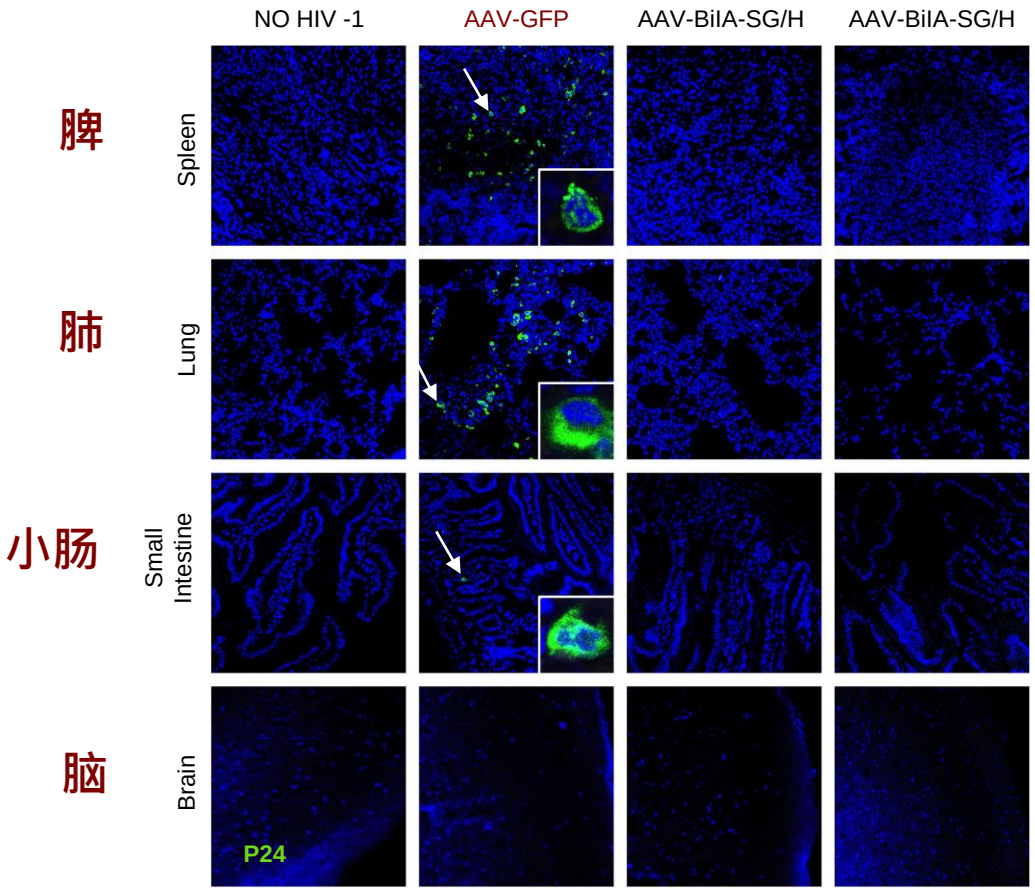
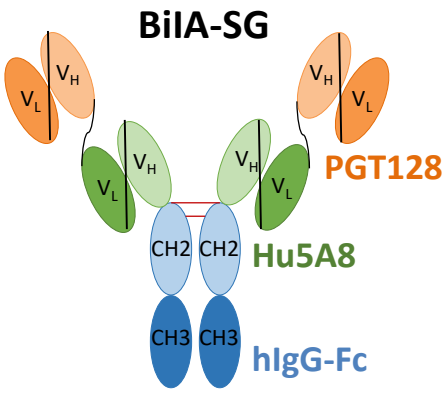


總結
Summary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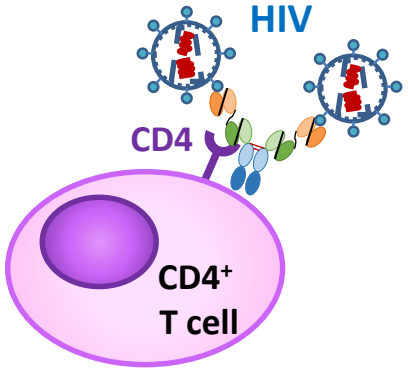
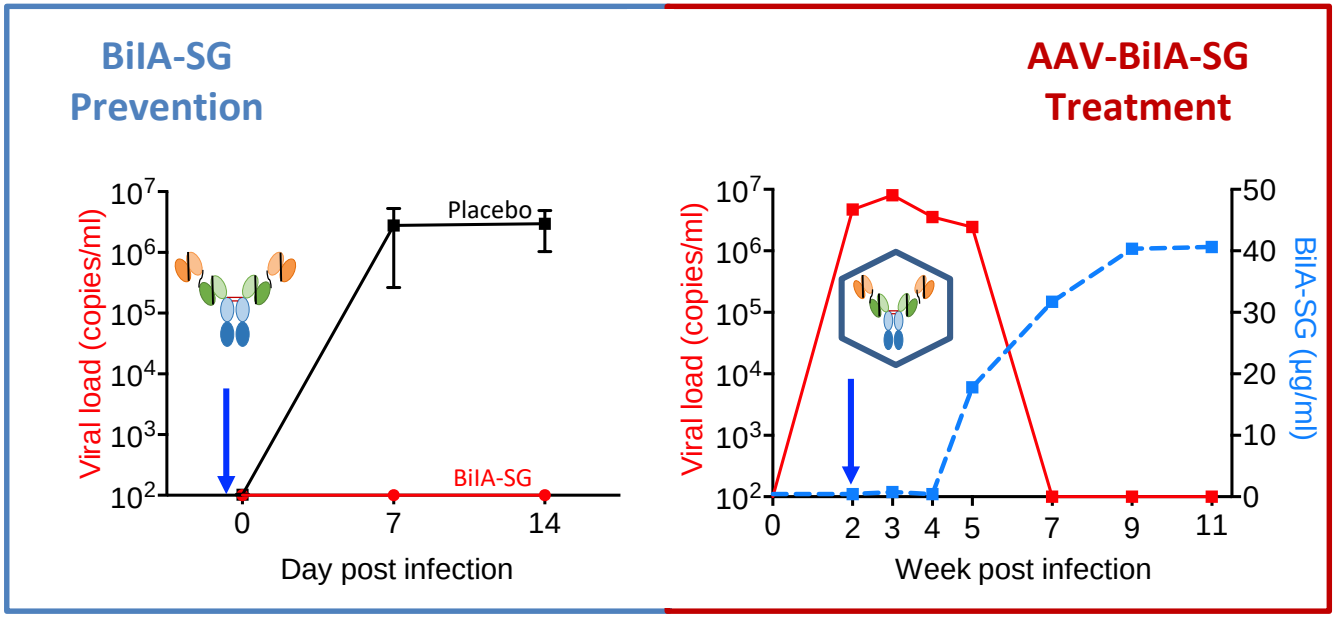
VH
VL
PGT128
CH2
Hu5A8
CH3
hIgG-Fc

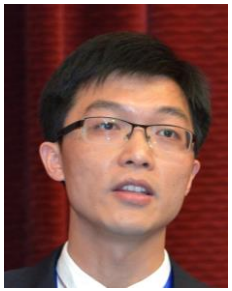

HIV
CD4
CD4+
T cell


BiIA-SG
Prevention
AAV-BiIA-SG
Treatment
Viral load (copies/ml)
Placebo
BiIA-SG
Day post infection
BiIA-SG (μg/ml)
Week post infection

致謝
Acknowledgement





並與深圳第三人民醫院王輝醫生、沈陽中國醫科大學尚紅教授、上海巴斯德研究所金俠教授、周保罗教授，以及清華大學張林琦教授合作

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