

**Pan-cancer study exploring the therapeutic role of FAP by transcriptomic, mutational and structural
bioinformatics approaches**

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Supplementary File 7A Binding affinity profile of lead compounds compared with LAF-237 across all protein targets

Lead Molecules	FAP		FAP_S576V		FAP_G581S		FAP_I620M		FAP_S624A		FAP_G666C		Average BE (kcal/mol)	Average IC (μM)
	BE (kcal/mol)	IC (μM)	BE (kcal/mol)	IC (μM)	BE (kcal/mol)	IC (μM)	BE (kcal/mol)	IC (μM)	BE (kcal/mol)	IC (μM)	BE (kcal/mol)	IC (μM)		
Lead 16	-6.07	35.25	-7.26	4.73	-6.76	11.06	-7.17	5.55	-7.31	4.39	-6.68	12.67	-6.87	12.27
Lead 8	-6.71	12.13	-6.8	10.44	-7.01	7.31	-6.44	18.91	-6.39	20.59	-6.66	13.02	-6.66	13.73
Lead 21	-5.93	45.32	-6.14	31.75	-6.32	23.14	-6.36	21.8	-6.27	25.55	-6.56	15.58	-6.26	27.19
Lead 29	-6.36	21.62	-5.9	47.16	-6.01	39.06	-6.01	39.31	-5.95	43.16	-6.24	26.63	-6.07	36.15
Lead 17	-5.51	92.06	-6.01	39.25	-6.07	35.73	-6	39.7	-6.47	18.04	-6.21	28.25	-6.04	42.17
LAF-237	-7.13	5.9	-7.12	6.08	-7.01	7.3	-7.11	6.19	-7.19	5.39	-7	7.37	-7.09	6.37

Supplementary File 7B Intermolecular interaction profiles of screened molecules with FAP and mutants

Protein target	Lead molecules	Protein binding residues				
		H-bond	van der Waals	Carbon-Hydrogen	Pi-alkyl & alkyl	Pi-Sigma
FAP	LAF-237	HIS734 , VAL540	GLN539, GLY622, GLY626, GLY735	SER624 , TRP623	TRP621, TYR541, HIS734 , TRP623	
	Lead16	GLN539, ASN556	TRP557, VAL540, GLY626, GLY622, HIS734	SER624 , TYR745	TRP621, ILE558, TYR541	TRP623
	Lead 8	GLN539	LEU571, SER548, ASN556, TRP557, TYR745, VAL540, GLY622, TRP623		ILE558, TYR541	TRP621
	Lead 21	TRP623	ARG123, GLY735, SER548, GLY626, GLN539, VAL540, GLY622, SER624		TYR541, HIS734	TRP621
	Lead 29	SER624 , HIS734 , GLU203	TYR656, ASN704, ARG123, GLU204, TYR660		TRP623, PHE350	
	Lead 17	TYR541, HIS734 , SER624 , ARG123	GLY735, TYR660, PHE350, TYR656, GLU203, ASN704		TYR541, TRP623, HIS734	TRP623
FAP_G576V	LAF-237	TYR660, TRP623, TYR656	SER546, GLY543, TYR541, GLY626, SER624 , PRO544, TYR625, PHE350, ASN704, GLU203, ARG123, GLU204			
	Lead16	TYR625, PRO544, SER624 , HIS734 , TYR660	CYS545, PHE350, ASN704, ARG123, GLY543	SER546, SER624	TYR656, VAL650, VAL705, TRP653	
	Lead 8	TYR625, TRP623, TYR660	HIS734 , TYR541, GLY626, GLY543, PRO544, PHE350, ARG123	SER624	TYR656, VAL705, VAL650, TRP653	
	Lead 21	ARG123	PHE350, GLY543, TYR625, SER546, GLY626, TRP623,		TYR656, TYR660, VAL705, TYR541	HIS734

			SER624 , ASN704, VAL650, PRO544			
	Lead 29	TYR660, TRP623	PHE350, PRO544, SER546, GLY543, TYR625, GLY626, ARG123, SER624 , ASN704, VAL705, TRP653		TYR541, HIS734 , VAL650	TYR656
	Lead 17	TYR625, HIS734 , ARG123	TRP653, ASN704, TRP623, GLY626, GLY543, SER546, GLU204	SER624	PHE350, TYR660, VAL650, VAL705, TYR656, TYR541	
FAP_G581S	LAF-237	TRP623, TYR656, TYR660	GLY543, SER546, TYR541, GLY626, TYR625, SER624 , ARG123, GLU203, GLU204		PHE350	
	Lead 16	PRO544, TYR656, TYR660	CYS545, TYR625, TYR541, SER624 , ASN704, GLU204, GLU203, ARG123	SER546, TYR660	PHE350, HIS734 , VAL705, VAL650, TYR656	
	Lead 8	TRP623, TYR625, TYR656, TYR660	GLY627, TYR541, PRO544, ARG123, PHE350, GLU204, GLY543	SER624	VAL705, HIS734 , VAL650, TRP653	
	Lead 21	HIS734 , ARG123, SER624 , TYR660	ASN704, VAL650, PRO544, SER546, GLY543, TYR541, GLY626, TRP623, TYR625		VAL705, TYR656, PHE350	TYR660
	Lead 29	TYR656, GLU204, ARG123	ASN704, HIS734 , PRO544, SER546, TRP623, GLY626, SER624 , TYR625, PHE350, GLU203	GLY543	TYR660, TYR541	
	Lead 17	TYR625, SER624 , HIS734 , ARG123	GLY626, TRP623, VAL705, VAL650, TRP653, SER546, GLY543	SER624	TYR541, TYR656, TYR660	
FAP_I620M	LAF-237	TRP623, TYR660, TYR656	GLY626, SER624 , TYR625, TYR541, SER546, GLY543, PRO544, PHE350, ARG123, ASN704, GLU203, GLU204			

	Lead 16	PRO544, TYR625, HIS734 , SER624 , TYR660	CYS545, ASN704, ARG123, GLY543	SER546	PHE350, TRP653, VAL650, VAL705	TYR656
	Lead 8	GLY543, SER546, ARG123	GLY542, TYR541, GLY626, TRP623, PRO544, TYR625, SER624 , ASN704, HIS734 , VAL705, VAL650		PHE350, TYR660, TYR656	
	Lead 21	HIS734 , SER624 , ARG123, TYR660	ASN704, VAL650, SER546, PRO544, GLY543, TYR541, GLY626, TRP623, TYR625		VAL705, TYR656, PHE350	
	Lead 29	SER546, TYR625, TRP623, ARG123	TYR541, GLY626, PHE350, HIS734 , SER624 , ASN704, GLY543	TYR660	VAL650, VAL705, TYR656	
	Lead 17	ARG123	SER624 , GLY543, SER546, GLY626, TRP623, TYR625, GLU204	TYR656	PHE350, TYR660, HIS734 , VAL650, VAL705, TYR541	
FAP_S624A	LAF-237	TYR656, TYR660, TRP623	SER546, GLY543, GLY626, ARG123, GLU203, GLU204		PHE350, TYR541, TYR625, ALA624	
	Lead16	TYR660, ARG123, TRP623	GLU203, GLU204, PHE350, TYR625, GLY543, SER546, TYR541		VAL650, ALA624 , HIS734 , VAL705	TYR656
	Lead 8	HIS734 , TYR660, TYR625		ARG123, PRO544, TRP653, GLY543, SER546, GLY626, TRP623	ALA624 , VAL705, VAL650, TYR656, TYR541	
	Lead 21	ARG123, HIS734 , TYR660	TRP623, GLY626, TYR541, GLY543, SER546, PRO544, VAL650, ASN704, TYR625		ALA624 , VAL705, TYR656, PHE350	

	Lead 29	TYR660, TRP623	PHE350, PRO544, GLY543, SER546, GLY626, ARG123, HIS734 , ASN704, VAL705, TRP653		VAL650, TYR625, ALA624 , TYR541	TYR656
	Lead 17	TYR660, GLY543	TRP653, TYR625, VAL705, HIS734 , TYR541, GLY542, SER546		ALA624 , TYR656, VAL650, PRO544	PHE350
FAP_G666C	LAF-237	TYR656, TYR660, TRP623	ARG123, GLU203, GLU204, GLY543, SER546, SER624		PHE350, TYR541, TYR625	
	Lead16	HIS734 , ARG123, TRP623	SER546, GLY543, TYR625, SER624 , GLY626, GLY627, TRP653	TYR656	TYR660, VAL650, VAL705, PHE350, TYR541	
	Lead 8	TYR660, GLY543, SER546, ARG123	VAL650, VAL705, ASN704, SER624 , TYR625, TRP623, GLY626, TYR541, GLY542, PRO544		PHE350, TYR656, HIS734	
	Lead 21	TRP623, TYR625, HIS734 , SER624	ASN704, GLY626, VAL705, VAL650, PHE350, SER546, PRO544, GLY543	TYR656	TYR541	TYR660
	Lead 29	GLU204, HIS734	PHE350, PRO544, TYR625, TYR660, TYR656, ASN704, ARG123, VAL705, SER624 , GLY543, TYR541, SER546			
	Lead 17	ARG123, TYR625, HIS734	GLU203, GLU204, PHE350, SER546, GLY626, TRP653, TRP623, TYR660, ASN704, GLY543	SER624	VAL650, VAL705, TYR541, TYR656	

*Amino acid residues in bold indicate catalytic triad residues