

# Discovery of Sulfated Small Molecule Inhibitors of Matrix Metalloproteinase-8

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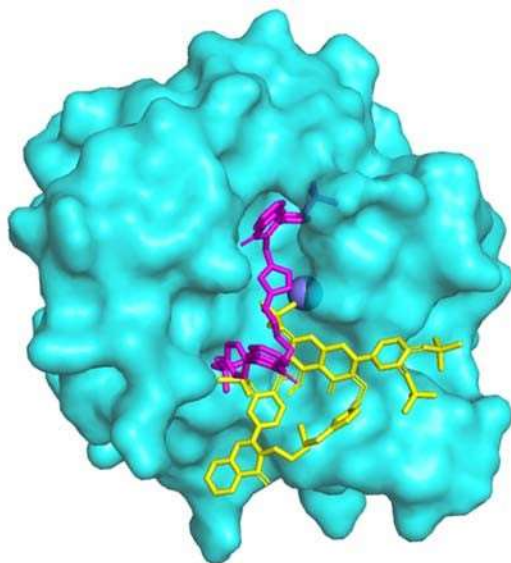
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**Table S1: General structure of MMP-8 inhibitors developed to date.**

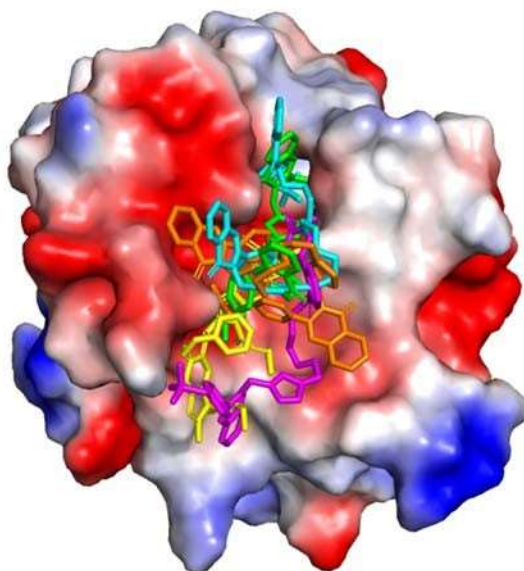
Compound class	Zinc-binding groups	General structure
Peptide hydroxamates [1]	Hydroxamate	
Peptide phosphonates [2-7]	Phosphonate	
Peptide thiolates [8]	Thiolate	
Sulfonamide phosphates [9]	Phosphonate	
Dihydropyrazothiazoles [10]	-	
Thienopyrimidinones [11]	-	

**Table S2: List of interactions made by NSGMs with MMP-8.**

<b>NSGM</b>	<b>Hydrogen &amp; ionic interactions</b>	<b>Non-bonded interactions</b>
26	H197, H201, H207, S151, Zn <sup>+2</sup>	E198, Q165, A163, F164, I170, D149, N150, I159, H162, A161
38	L160, A163, L193, L214, P217, A220, R222	V194, N218, G158, L160, I159, S151, F164, A163, H162, H207, H197, A161, E198, Y216
40	H197, H201, H207, Zn <sup>+2</sup> , Q165, N150, E198	P217, A163, G171, F164, N150, N85
41	E198, H197, H201, H207, Zn <sup>+2</sup> , H162, S151	I159, E198, P152, F164, A163
42	E198, H197, H201, H207, Zn <sup>+2</sup> , N157	P217, L160, V194, Y219, H197, E198, H162, I159, N218, G158



**Figure S1:** Comparison of the mode of binding of **38** and **43** on MMP-8. The bulk of tetra-sulfated quercetin does not allow its placement in the S<sub>1</sub>' pocket, resulting in loss of inhibition of heterodimeric NSGMs **43–46**.



**Figure S2:** Mode of binding of the top five NSGM inhibitors (**26**, yellow; **38**, green; **40**, magenta; **41**, orange; **42**, cyan – in sticks) of MMP-8 (shown in ESP map).

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