Electronic Supplementary Information

Inhibition of FAD-dependent lysine-specific demethylases by chiral polyamine analogues.

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Table of Contents
1. ¹H-NMR and ¹³C-NMR charts of novel polyamines 8-15
2. HPLC charts of novel polyamines 8-15
3. Fo-Fc electron density maps and X-ray absorption fine structure (XAFS) spectroscopy of the LSD1·CoREST complexes soaked with polyamines
4. The molecular docking simulation of polyamine 2 against the LSD1 crystal structure
5. Lineweaver-Burk plot in the presence and absence of polyamine 13
6. Kinetic analysis of LSD1 demethylation activities by polyamines 1, 2, 5, 6 and 8-15
7. Kinetic analysis of LSD2 demethylation activities by polyamines 2 and 9-15
8. Kinetic analysis of MAO-A oxidation activities by polyamines 2 and 9-15
9. Kinetic analysis of MAO-B oxidation activities by polyamines 2 and 9-15
1. $^1$H-NMR, $^{13}$C-NMR, HPLC charts of novel polyamines 8-15

- Polyamine 8 [RS-RS-RS]
• Polyamine 9 [RS-RS-SR]

\(^1\)H-NMR

\(^{13}\)C-NMR
• Polyamine 10 [RS-SR-RS]

$^1$H-NMR

$^{13}$C-NMR
• Polyamine 11 [SR-RS-RS]

$^1$H-NMR

$^{13}$C-NMR
Polyamine 12 [SR-SR-SR]

\[ ^{1}H\text{-NMR} \]

\[ ^{13}C\text{-NMR} \]
• Polyamine 13 [SR-SR-RS]

$^1$H-NMR

$^{13}$C-NMR
• Polyamine 14 [SR-RS-SR]

$^1$H-NMR

$^{13}$C-NMR
• Polyamine 15 [RS-SR-SR]

$^1$H-NMR

$^{13}$C-NMR
2. **HPLC charts of novel polyamines 8-15**

   Conditions: All traces were monitored at 220 nm. Flow rate: 1.0 mL/min

   Linear gradient system from 10:90 to 80:20 CH$_3$CN / H$_2$O (0.1% TFA) over 70 min (polyamine 8)

   Linear gradient system from 10:90 to 70:30 CH$_3$CN / H$_2$O (0.1% TFA) over 60 min (polyamines 9-15)

- Polyamine 8 [$RS$-$RS$-$RS$]

- Polyamine 9 [$RS$-$RS$-$SR$]
• Polyamine 10 [RS-SR-RS]

• Polyamine 11 [SR-RS-RS]

• Polyamine 12 [SR-SR-SR]
• Polyamine 13 [SR-SR-RS]

• Polyamine 14 [SR-RS-SR]

• Polyamine 15 [RS-SR-SR]
3. Fo-Fc electron density maps and X-ray absorption fine structure (XAFS) spectroscopy of the LSD1·CoREST complexes soaked with polyamines

Figure S1. Fo-Fc electron density maps surroundings substrate binding site and X-ray absorption fine structure (XAFS) spectrogram of the LSD1·CoREST complexes soaked with polyamines. Green and Red density maps (3.5 σ level) represent positive and negative, respectively. (A) An Fo-Fc map of an LSD1·CoREST complex soaked with H3(1–20)K4me2 peptide. (B) An Fo-Fc map of an LSD1·CoREST complex soaked with polyamine 2. (C) An X-ray absorption fine structure (XAFS) spectrogram of an LSD1·CoREST complex soaked with polyamine 8. (D) An Fo-Fc map of an LSD1·CoREST complex soaked with polyamine 8.
4. The molecular docking simulation of polyamine 2 against the LSD1 crystal structure

Figure S2. Representative binding models of polyamine 2 in the LSD1 catalytic cavity were predicted by computational modeling. Fo-Fc density map of an LSD1•CoREST complex soaked with polyamine 2 around substrate binding site contoured at 3.5 σ level.
5. Lineweaver-Burk plot in the presence and absence of polyamine 13

Figure S3. Lineweaver–Burk plot of competitive inhibition model for polyamine 13 with variable concentrations of the H3(1–20) K4-dimethylated (K4me2) peptide substrate.
6. Kinetic analysis of LSD1 demethylation activities by polyamines 1, 2, 5, 6 and 8-15
Figure S4. Kinetic analysis of LSD1 demethylation activities by polyamines. The plots (mean ± SE; N=3) are made using the LSD1 demethylation activities at 10 min after the reaction. The solid lines are from the non-linear regression according to the equation of competitive inhibition via steady-state kinetic analysis.
7. Kinetic analysis of LSD2 demethylation activities by polyamines 2 and 9-15
Figure S5. Kinetic analysis of LSD2 demethylation activities by polyamines. The plots (mean ± SE; N=3) are made using the LSD2 demethylation activities at 10 min after the reaction. The solid lines are from the non-linear regression according to the equation of competitive inhibition via steady-state kinetic analysis.
8. Kinetic analysis of MAO-A oxidation activities by polyamines 2 and 9-15
Figure S6. Kinetic analysis of MAO-A oxidation activities by polyamines. The plots (mean ± SE; N=3) are made using the MAO-A oxidation activities at 10 min after the reaction. The solid lines are from the non-linear regression according to the equation of competitive inhibition via steady-state kinetic analysis.
9. Kinetic analysis of MAO-B oxidation activities by polyamines 2 and 9-15

2 [RS-RS-RS]

9 [RS-RS-SR]

10 [RS-SR-RS]

11 [SR-RS-RS]

12 [SR-SR-SR]

13 [SR-SR-SR]
Figure S7. Kinetic analysis of MAO-B oxidation activities by polyamines. The plots (mean ± SE; N=3) are made using the MAO-B oxidation activities at 30 min after the reaction. The solid lines are from the non-linear regression according to the equation of competitive inhibition via steady-state kinetic analysis.