Title

Explaining RANKL inhibition by OPG through quantum biochemistry computations and insights into peptide-design for the treatment of osteoporosis

Authors

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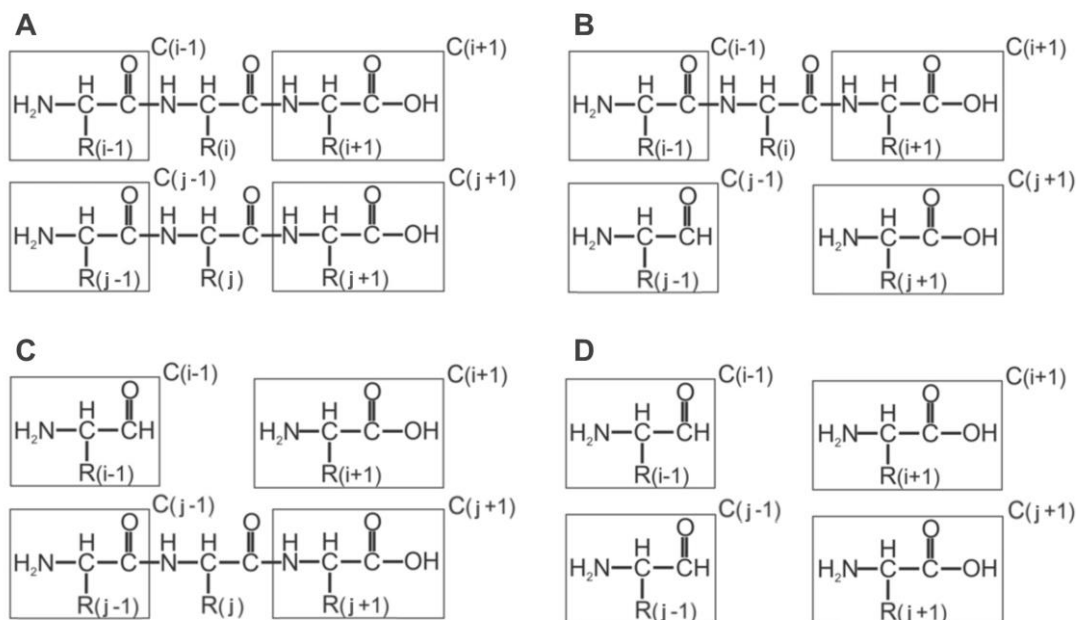
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The following supplementary information accompanies the manuscript:

- **Supplementary Figure S1** – MFCC scheme representing the four distinct fragment systems employed to calculate the interaction energies between the analysed residues.

- **Supplementary Figure S2** – Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all interactions established between RANKL and OPG at site I, applying treatment 2.

- **Supplementary Figure S3** – BIRD panel showing the MFCC interaction energy for all OPG's amino acid residues involved in site I, applying treatment 2.

- **Supplementary Figure S4** – BIRD panel showing the MFCC interaction energy for all interactions established between RANKL and OPG at site II, applying treatment 2.

- **Supplementary Figure S5** – BIRD panel showing the MFCC interaction energy for all OPG's amino acid residues involved in site II, applying treatment 2.

- **Supplementary Figure S6** – BIRD panel showing the MFCC interaction energy for all amino acid residues from RANKL-A, applying treatment 1.

- **Supplementary Figure S7** – BIRD panel showing the MFCC interaction energy for all amino acid residues from RANKL-B, applying treatment 1

- **Supplementary Figure S8** – BIRD panel showing the MFCC interaction energy for all amino acid residues from RANKL-A, applying treatment 2

- **Supplementary Figure S9** – BIRD panel showing the MFCC interaction energy for all amino acid residues from RANKL-B, applying treatment 2.

# SUPPLEMENTARY INFORMATION

FIGURES

Supplementary Figure S1. MFCC scheme representing the four distinct fragment systems employed to calculate the interaction energies between the analysed residues: (A) system formed by the two interacting residues with conjugated caps; (B) system formed by residue Ri with conjugated caps and the hydrogenated caps of residue Rj; (C) system formed by residue Rj with conjugated caps and the hydrogenated caps of residue Ri; (D) system formed by hydrogenated caps only. The analysed residues and the conjugated caps are represented as R and C, respectively.
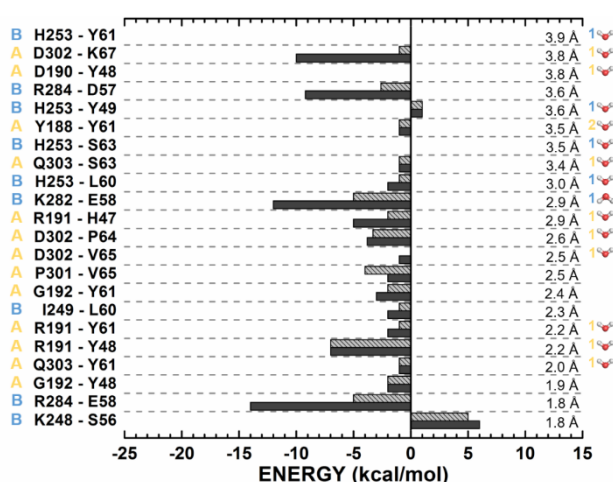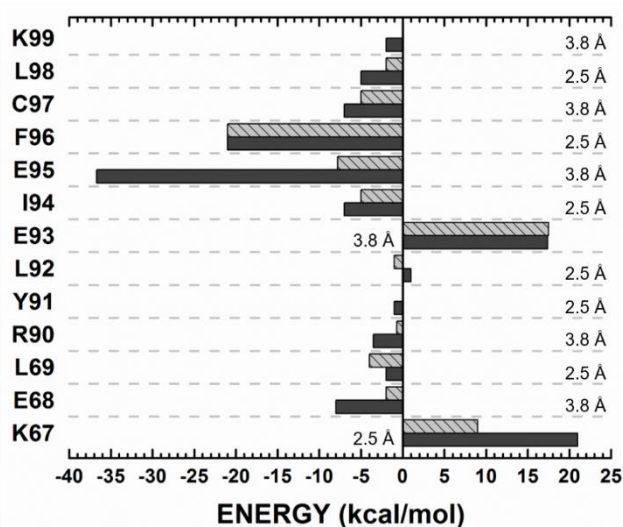

Supplementary Figure S2. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all interactions established between RANKL and OPG at site I, applying treatment 2. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. Colored letters at the left side of the panel assign the RANKL unit involved for each interaction. The distance and the number of water molecules involved for each interaction are presented at the right side of the panel. Numbers disposed at the left side of the water representation are related to RANKL residues, while numbers disposed at the right side are related to OPG residues.
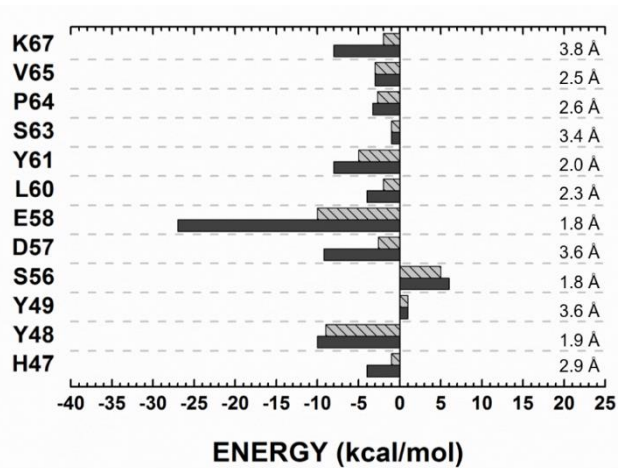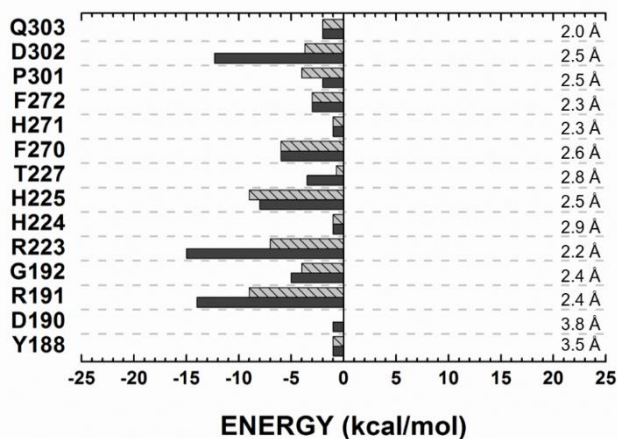
Supplementary Figure S3. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all OPG's amino acid residues involved in site I, applying treatment 2. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. The distance of each interaction is presented at the right side of the panel.
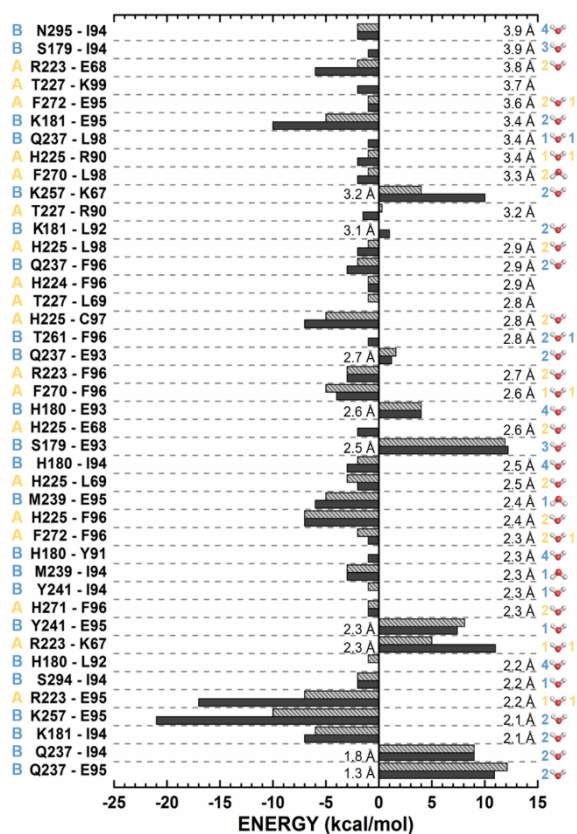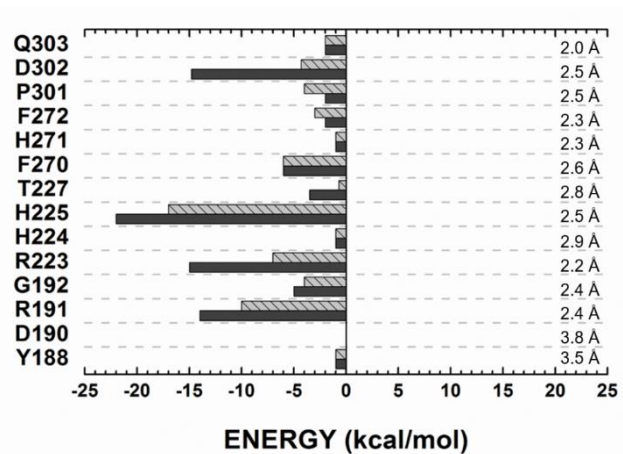

Supplementary Figure S4. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all interactions established between RANKL and OPG at site II, applying treatment 2. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. Colored letters at the left side of the panel assign the RANKL unit involved for each interaction. The distances related to attractive and repulsive interactions are presented at the right side and at the central part of the panel, respectively. The water molecules involved at each interaction are represented at the right side of the panel, with numbers disposed at the left of the water representation side related to RANKL residues and numbers disposed at the right side related to OPG residues, respectively.
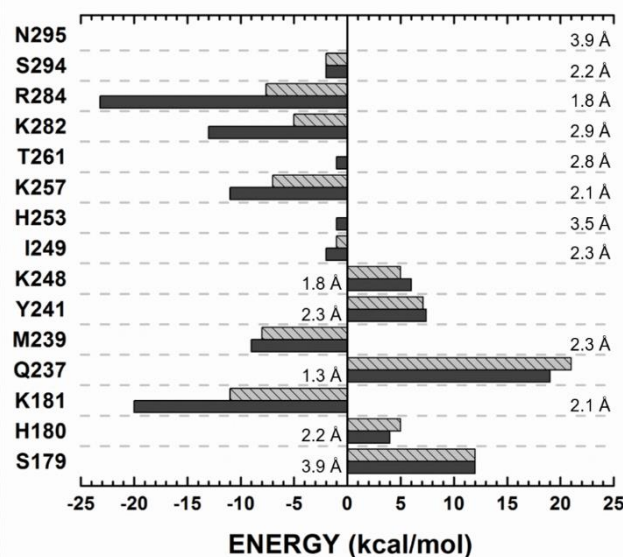
Supplementary Figure S5. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all OPG's amino acid residues involved in site II, applying treatment 2. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. The distances related to attractive and repulsive interactions are presented at the right side and at the central part of the panel, respectively.
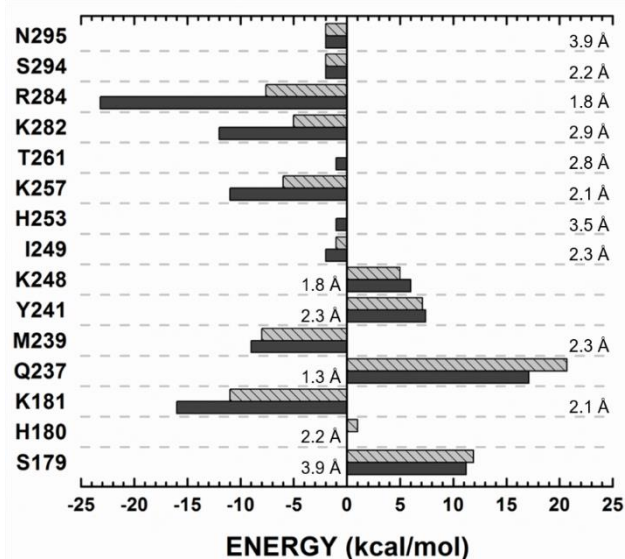

Supplementary Figure S6. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all amino acid residues from RANKL-A, applying treatment 1. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. The distance of each interaction is presented at the right side of the panel.

Supplementary Figure S7. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all amino acid residues from RANKL-B, applying treatment 1. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. The distances related to attractive and repulsive interactions are presented at the right side and at the central part of the panel, respectively.

Supplementary Figure S8. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all amino acid residues from RANKL-A, applying treatment 2. Dark and light grey bars represent values obtained with ε=10 and ε=40, respectively. The distance of each interaction is presented at the right side of the panel.

Supplementary Figure S9. Binding site, interaction energy and residues domain (BIRD) panel showing the MFCC interaction energy for all amino acid residues from RANKL-B, applying treatment 2. Dark and light grey bars represent values obtained with $\varepsilon=10$ and $\varepsilon=40$, respectively. The distances related to attractive and repulsive interactions are presented at the right side and at the central part of the panel, respectively.