11-9-2018

Directly Targeting HIF Activity Controls FGF23 Expression Revealing Translational Considerations for CKD-related Anemia

Julia Hum Ph.D  
*Marian University - Indianapolis*

Bryan Wacker OMS-1  
*Marian University - Indianapolis*

Vince Marshall OMS-1  
*Marian University - Indianapolis*

Follow this and additional works at: https://mushare.marian.edu/mucom_rd

Part of the Medicine and Health Sciences Commons

Recommended Citation


https://mushare.marian.edu/mucom_rd/107

This Poster is brought to you for free and open access by the College of Osteopathic Medicine at MUSHare. It has been accepted for inclusion in MUCOM Research Day by an authorized administrator of MUSHare. For more information, please contact emandity@marian.edu.
FG-4592 in vivo effects on FGF23 in WT mice

Figure 2. 8-week old female C57Bl6 WT mice were injected with increasing doses of FG-4592 (10 mg/kg – 80 mg/kg) i.p. every other day for 5 days for a total of 3 injections. (A) At the time of harvest, serum EPO was significantly increased in the 50, 70, and 80 mg/kg groups compared to vehicle. (B) Bone FGF23 mRNA expression was significantly upregulated in mice receiving the 80 mg/kg dose of FG-4592, while serum FGF23 levels were also significantly increased with the 50, 70, and 80 mg/kg dose compared to vehicle. (C) Bone FGF23 mRNA expression was significantly upregulated in mice receiving the 80 mg/kg dose of FG-4592, while serum FGF23 levels were also significantly increased with the 50, 70, and 80 mg/kg dose compared to vehicle. (D) Bone FGF23 mRNA expression was significantly upregulated in mice receiving the 80 mg/kg dose of FG-4592, while serum FGF23 levels were also significantly increased with the 50, 70, and 80 mg/kg dose compared to vehicle. (E) Bone FGF23 mRNA expression was significantly upregulated in mice receiving the 80 mg/kg dose of FG-4592, while serum FGF23 levels were also significantly increased with the 50, 70, and 80 mg/kg dose compared to vehicle. (F) Bone FGF23 mRNA expression was significantly upregulated in mice receiving the 80 mg/kg dose of FG-4592, while serum FGF23 levels were also significantly increased with the 50, 70, and 80 mg/kg dose compared to vehicle.

Mice on adenine diet decrease levels of TNFα but have no effect on IL-6

Figure 4. 10-week old female C57Bl6 WT mice were placed on either a casein control diet or an adenine-containing diet to induce CKD. After 8 weeks on diet and anemia established (see Figure 3), mice were injected with 70 mg/kg FG-4593 i.p. every other day for 5 days for a total of 3 injections. (A) TNFα was significantly decreased in the adenine diet mice compared to the casein diet controls. (B) IL-6 levels remained the same in both casein control and adenine treated mice, regardless of FG treatment. (**p<0.01 vs Casein at same time point)

FG-4592 induces FGF23 mRNA and stabilizes Hif-1α in human and murine osteoblast cells

Human U2OS

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>FG 20μM</th>
<th>FG 50μM</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGF23</td>
<td>0.14</td>
<td>0.16</td>
<td>0.18</td>
</tr>
<tr>
<td>TRC1</td>
<td>0.08</td>
<td>0.10</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Mouse MPC-2

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>FG 20μM</th>
<th>FG 50μM</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGF23</td>
<td>0.14</td>
<td>0.16</td>
<td>0.18</td>
</tr>
<tr>
<td>TRC1</td>
<td>0.08</td>
<td>0.10</td>
<td>0.12</td>
</tr>
</tbody>
</table>

SUMMARY & CONCLUSIONS

• FG-4592 induced FGF23 mRNA expression in both human and murine osteoblast/osteocyte-like cell lines
• WT mice treated with FG-4592 increased serum EPO and FGF23, as well as bone, marrow, spleen, and liver FGF23 RNA
• The adenine diet induces renal failure with associated anemia and markedly increases FGF23
• The HIF-PHI FG-4592 increases endogenous EPO production to potentially reverse anemia, thus lowering FGF23 to improve clinical outcomes for CKD patients

ACKNOWLEDGMENTS

NIAMS & NIDDK