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**Identification of Small Molecule Modulators of the Hv1 Proton Channel**

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The human voltage-gated proton channel (hHV1) plays an important role in immune and cancer cells being involved in a variety of patho-physiology of the cells. HV1, contrary to the other voltage-gated ion-channels does not have a conventional ion-conducting pore, the conduction occurs through the voltage-sensing domain. This difference may be the reason for the lack of selective hHV1 inhibitors. Currently, 5-chloro-2-guanidinobenzimidazole (ClGBI) is the most widely used inhibitor of HV1 (IC50 ≈ 26 μM), however, it presents a low selectivity for the channel. This could lead to misinterpretation of functional assays addressing the role of HV1. Thus, our aim is to find potent and more selective inhibitors for hHV1, which could be useful research tools and serve as lead molecules for the development of drug molecules targeting HV1 for therapeutic goals. We used manual patch-clamp whole cell configuration and measured on transfected CHO model cells, using small molecules inhibitors synthesized from our pharmaceutical chemist collaborators in Slovenia. Our results showed several molecules that effectively blocked the channel in which compound named GHK30 had an IC50 ≈ 13 μM and showed to be the most selective over Kv1.3 potassium channel among others potent molecules and were further selected to understand its biophysical mechanism of action on hHV1.