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Generation of a Peptide Library from human Bone Marrow for the discovery and identification of novel bio active bone-marrow derived peptides

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Human bone marrow contains an abundance of proteins and peptides that are essential for the formation of blood cells. Thus, bone marrow is expected to contain a wealth of factors that influence cell growth, differentiation, and function. Aiming to identify novel bioactive peptides in human bone marrow, we established a method to generate a peptide library from primary human material. To this end, 25 kilograms of human bone (femur) from donors were collected, and the bone marrow was extracted. The eluted peptides were separated into 285 fractions, and consecutively tested for bioactivity e.g. immune modulation, cell viability and growth, and anti-viral activity. After further iterative bioassay guided sub-fractionation, peptides responsible for the function can be identified. In summary, our data show that human bone marrow contains peptides that modulate autophagy and inhibit viral infections. This project provides the basis for establishing peptide extraction methods from complex human tissues to identify novel peptide modulators of cellular processes.

Generation of the Peptide Library

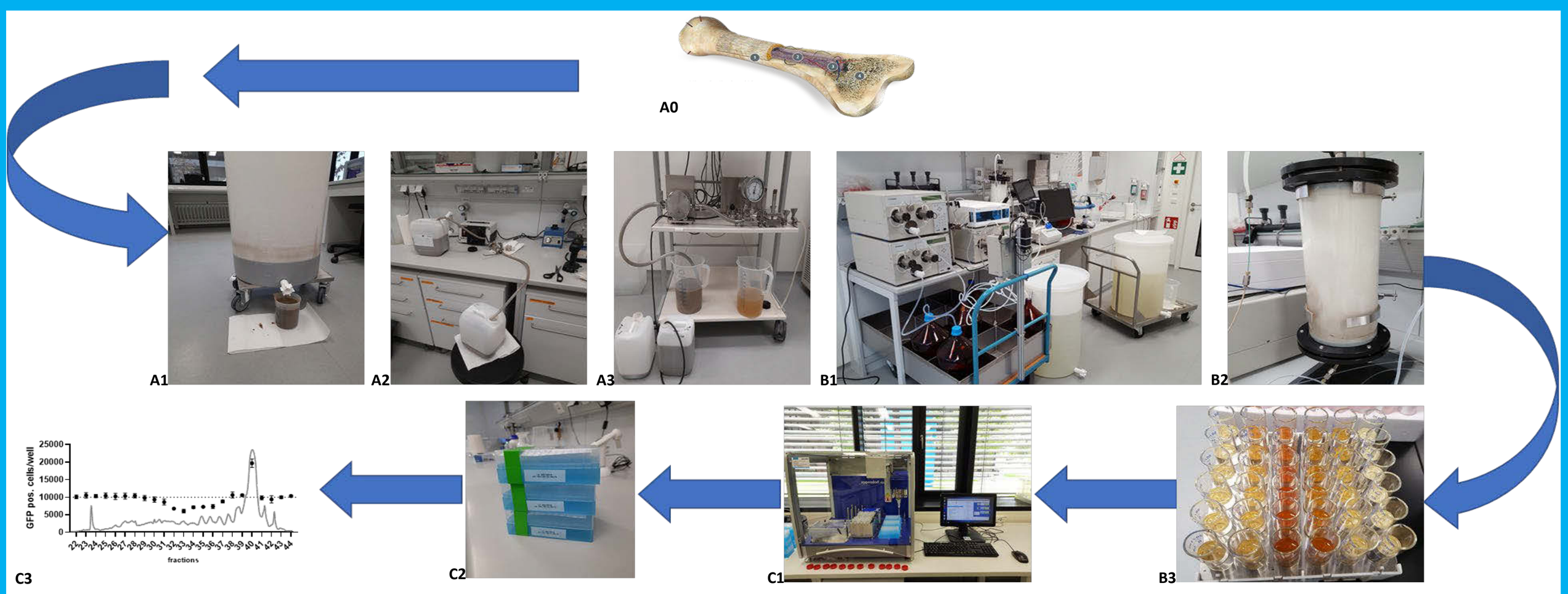

Figure 1: A0-3 Generation of a peptide library from human Bone Marrow. **A0**: Schematic representation of a human bone depicting bone marrow extraction sites(2).**A1-3:** Bone marrow peptide extraction, filtration, and ultrafiltration (cutoff 30kDa).
B1-3 Capture and fractionation of the ultrafiltered peptides, by CEX and RPC. **C1-3** Aliquotation of the mother fractions, assembling aliquots for client/collaborator use of the peptide library, screening of the peptide library for active fractions in partner institutes.

Screening for Bioactive Fractions

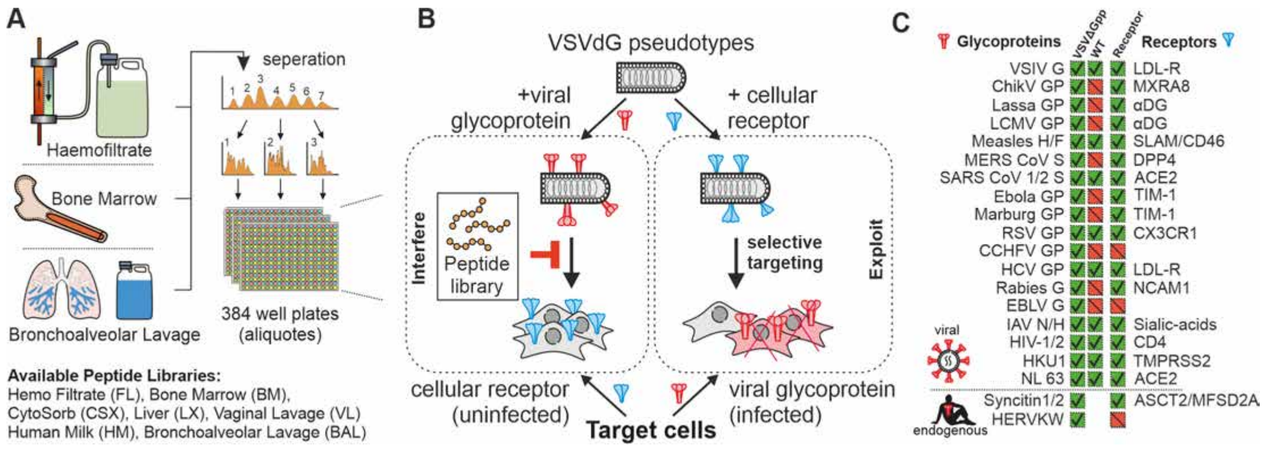

Figure 2: A Schematic depiction of the generation of human-derived peptide libraries. **B** Outline of the two major strategies of the project: Interfere (left) and Exploit (right).
C List of the already established Vesicular Stomatitis Indiana Virus ΔG pp, as well as corresponding wild type viruses and, if identified, their receptors.

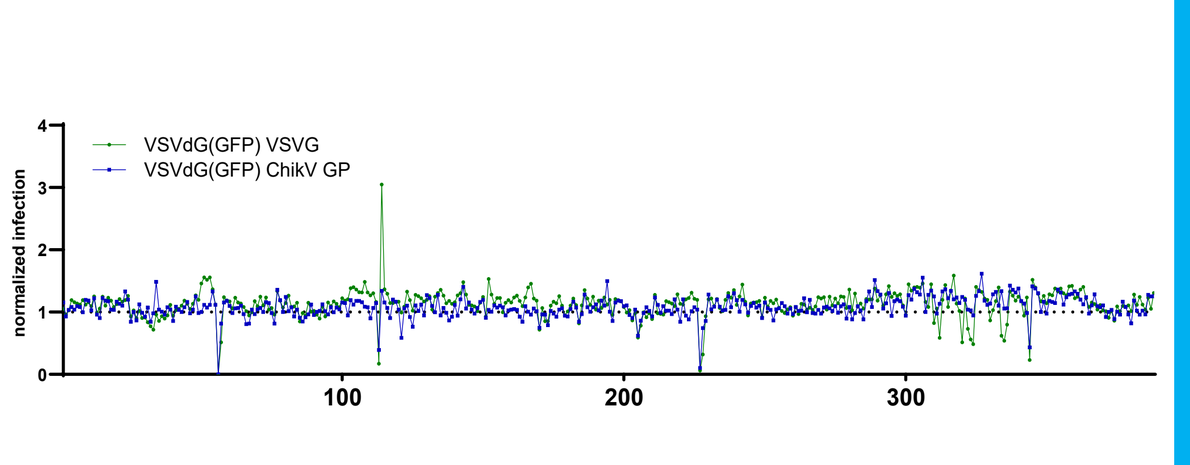

Figure 3: Isolation of candidate peptides that selectively inhibit Chikungunya virus GP-mediated infection**.** A Full proof-of-concept dual-colour screen, of the bone marrow peptide library including over 350 wells.

References:

- Kaygisiz, K. et al. Data-mining unveils structure-property-activity correlation of viral infectivity enhancing self-assembling peptides. Nat. Commun. 14, 5121 (2023)
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- Logo 37th EPS https://eps2024.com/

DFG Deutsche Forschungsgemeinschaft

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Summary and Perspectives

- Human bone marrow-derived peptides were extracted and collected
- A human bone marrow peptide library was generated.
- The peptide library was screened for autophagy modulation and activity against different viral glycoproteins
  - → Chromatographic purification of the active peptides.
  - → Mass spectrometry and sequencing of the pure peptides.
  - → Identification of the active peptides and testing synthetic variants of them.