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RESEARCH AREA

1. Interleukin-2 and -15 receptor function
Interleukin-2 and -15 are cytokines that play a key role in the regulation of T lymphocyte life processes. IL-2 is responsible for the expansion of T cells clones specific for a pathogen, and for the apoptotic cell death of T cells after elimination of the infection. It also plays an important role in maintaining peripheral immune tolerance. IL-15, on the other hand, inhibits apoptosis and is responsible for the long-term survival of memory T cells and thus for the development of immunological memory. Both cytokines and their receptors play a role in lymphoma and autoimmune diseases and in the anti-cancer immune response, thus serving as drug targets or adjuvants.
Our aims:
a) To elucidate the molecular basis of immunological memory by investigating the appearance and role of the IL-15 receptor in the cell nucleus.
b) We have shown that the IL-2 receptor is preassembled and signals inside the cell, and that this intracrine signalling explains the ineffectiveness of antilymphoma antibody therapies. We are investigating the mechanism of intracrine signalling and would like to extend the investigation of this phenomenon to additional membrane receptors.

2. Investigating the function of nuclear receptors
Nuclear receptors are dimeric transcription factors that activate in the presence of a ligand and inhibit in the absence of their ligand the transcription of their target genes. They regulate many biological processes, such as cell division, differentiation, cell death, metabolism and immune responses. Therefore, about 10% of all prescribed drugs target nuclear receptors. The repression or activation complex is composed of the nuclear receptor dimer, the ligand(s), the corepressor or coactivator protein and the DNA response element located in the regulatory region of the target gene. We study their assembly using modern fluorescence microscopy and genomic methods. Based on our previous studies, we have demonstrated the competition of nuclear receptors for genomic binding sites or for a common heterodimerization partner, which may explain the side effects of some ligand therapies targeting nuclear receptors.

TECHNIQUES AVAILABLE IN THE LAB

- confocal microscopy
- flow cytometry
- immunofluorescence labelling
- Förster resonance energy transfer
- fluorescence correlation spectroscopy
- cloning techniques
- PCR
- cell culture
- transfection
- gel electrophoresis
- Western blot

SELECTED PUBLICATIONS

Kenesei, Á., Volkó, J., Szalóki, N., Mocsár, G., Jambrovics, K., Balajthy, Z., Bodnár, B., Tóth, K., Waldmann, T.,A., **Vámosi, G.** (2021) IL-15 trans-presentation is an autonomous, antigen independent process. **J Immunol. 10:** 2489-2500.

Fadel, L., Rehó, B., Volkó, J., Bojcsuk, D., Kolostyák, Z., Nagy, G., Müller, G., Simándi, Z., Hegedüs, É., Szabó, G., Tóth, K., Nagy, L., **Vámosi, G.** (2020) Agonist binding directs dynamic competition among nuclear receptors for heterodimerizationwith retinoid X receptor. **J Biol Chem. 295:** 10045-10061.

Rehó, B., Lau, L., Mocsár, G., Müller, G., Fadel, L., Brázda, P., Nagy, L., Tóth, K., **Vámosi, G.** (2020) Simultaneous Mapping of Molecular Proximity and Comobility Reveals Agoni Enhanced Dimerization and DNA Binding of Nuclear Receptors. **Anal Chem. 92**: 2207-2215.

Volkó, J., Kenesei, Á., Zhang, M., Várnai, P., Mocsár, G., Petrus, M.,N., Jambrovics, K., Balajthy, Z., Müller, G., Bodnár, A., Tóth, K., Waldmann, T.,A., **Vámosi, G.** (2019) IL-2 receptors preassemble and signal in the ER/Golgi causing resistance to antiproliferative anti-IL-2Rα therapies. **Proc Natl Acad Sci USA. 42:** 21120-21130.

Nagy, É., Mocsár, G., Borbásné, Sebestyén, V., Volkó, J., Papp, F., Tóth, K., Damjanovich, S., Panyi, G., Waldmann, T., Dóczy-Bodnár, A., **Vámosi, G.** (2018) Membrane Potential Distinctly Modulates Mobility and Signalingof IL-2 and IL-15 Receptors in T Cells. **Biophys. J. 10:** 2473-2482.