Identification of galectin-1 as a critical factor in function of mouse mesenchymal stem cell-mediated tumour promotion

Gábor János Szebeni

Ph.D. thesis

Supervisor: Éva Monostori, Ph.D., D.Sc.
HAS Biological Research Centre, Institute of Genetics
Lymphocyte Signal Transduction Laboratory

Ph.D. School in Biology
University of Szeged, Szeged
2012
I. Introduction

In spite of the increasing significance, the origin of the tumour-associated non-tumour-cell elements (tumour-associated fibroblasts and endothelium) has not been determined decisively. As it has recently been shown, one source of the tumour-associated stroma (TAS) is bone marrow-derived mesenchymal stem cells (BM-MSCs) which migrate into the solid tumour and there contribute to the establishment of TAS.

Exogenously administered MSCs migrate and specifically localize into tumours. However, the effect of transplanted MSCs in term of tumour progression is still actively debated, since both tumour-promoting and tumour-moderating functions have been indicated. Tumour promotion by MSCs has been primarily attributed to their immunosuppressive function and neo-vascularisation promoting effect. All effects of MSCs in solid tumours can be explained by two mechanisms: 1) differentiation of the multipotent MSCs into tumour-associated tissue elements such as fibroblasts, tumour-associated blood vessel endothelium and/or smooth muscle or 2) MSCs are not stably associated with these sites, rather they affect tumorigenesis via producing various angiogenic (VEGF, PDGF, FGF), immunosuppressive (TGF-β, IDO, IL-10, PGE2) and metastatic (CCL5) factors. These possibilities are not exclusive; however providing definite answer is difficult due to the lack of MSC specific molecular markers.

Galectin-1 (Gal-1) is an immunosuppressive and pro-angiogenic member of the β-galactoside-binding lectin family, galectins. Immunosuppressive function of Gal-1 has been confirmed in a number of in vivo and in vitro studies. Targeted inhibition of Gal-1 function or expression in tumour cells provokes immune response against the tumour and subsequent tumour rejection. Also, Gal-1 has recently been implicated in growth and metastasis of solid tumours. Accordingly, high expression of Gal-1 in the tumour cells and/or in TAS indicates poor prognosis of the disease. Crucial role of Gal-1 in tumour angiogenesis has also been confirmed. Additionally, genetically engineered carcinoma-associated fibroblasts expressing low level of Gal-1 failed to help tumour progression. High level of Gal-1 expression has been detected in BM-MSCs contributing to the T-cell regulating role of MSC in vitro.

II. Aims

It was previously shown that MSCs produce Gal-1 but functional studies revealed only the in vitro immunosuppressive role of MSC derived Gal-1. The effect of MSCs on the development of solid tumours and the key factors released by MSCs influencing tumour progression remained unknown. In order to elucidate these questions we addressed the following:

1.) What is the impact of Gal-1 produced by bone marrow derived MSCs on the growth, vascularisation and metastatic frequency of primary tumours in animal model?
2.) How does the bone marrow MSC-derived Gal-1 influence the incidence of primary tumours and the survival of tumour bearing mice?
3.) How can be sequestered the effect of MSC or tumour cell derived Gal-1 on the development of cancer?
III. Methods

1. Isolation of MSCs
2. Mammalian cell culturing
3. Characterisation of MSCs by flow cytometry
4. Characterisation of adipogenic and osteogenic differentiation property of MSCs
5. Gal-1 gene silencing in MSCs by siRNA transfection
6. Mouse tumour models
7. SDS gel-electrophoresis and Western blot analysis
8. Histology
9. In vitro capillary formation assay
10. In vitro migration assay
11. Statistical analysis
12. Preparation of buffers, solutions

IV. Results

IV.1. Characterization of MSCs and tumour cell lines

All types of MSCs used in this study: wild type (wtMSC), Gal-1 knocked down (siMSC), control cells transfected with scrambled RNA (scMSC) and Gal-1 knockout (MSC Gal-1−/−) cells uniformly expressed CD44, CD73, CD90 and Sca-1 but not markers of hematopoietic cell origin, CD34, CD45R, Ly6G, CD3, CD11b, TER119 and differentiated into adipogenic and osteogenic directions. Western blotting analysis showed that wt and scMSCs expressed abundant, siMSCs low level and MSC Gal-1−/− none of Gal-1. Tumour cell lines, 4T1 breast carcinoma and B16F10 melanoma cells also expressed high level of Gal-1.

IV.2. MSCs localize within the tumour tissue irrespective of their Gal-1 production

To determine whether Gal-1 expression in MSCs contributed to the localization and survival of MSCs within the tumour environment, first an in vitro migration assay was carried out. Neither absence of Gal-1 in MSC Gal-1−/− nor reduction of Gal-1 in siMSCs affected the number of the migrating cells toward 4T1 cells. In contrast, the migration of MSCs significantly slowed down. There was no migration observed when MSCs were cultured alone in the migration plate. Analysis of the frozen tumour tissue sections obtained from animals co-injected with 4T1 breast carcinoma cells and fluorescent dye labelled wtMSCs or MSC Gal-1−/− showed no difference between the localization of the different MSCs. The siMSCs and scMSCs persisted in the tumour similarly to wtMSCs.

IV.3. Gal-1-dependent enhancement of tumour growth

Balb/C mice were injected with syngeneic 4T1 breast carcinoma cells with or without wtMSCs or MSCs Gal-1−/−. Tumour volume and weights were increased 3.5-fold and 4.5-fold, respectively by wtMSCs on the 40th day and the tumours were palpable much earlier (20th versus 32nd day) compared to that of induced by tumour cells alone. In contrast to wild type MSCs, co-injection of Gal-1 deficient MSC did not affect tumour development either in size, timing, or weight. Co-injection of siMSCs expressing low but detectable amount of Gal-1 or control scMSCs resulted in similar effects to that of wtMSCs indicating that low amount of
Gal-1 in MSCs was sufficient to exert tumour promoting effect. MSCs alone did not generate tumour development in 110 days follow up. Analysis of incidence of palpable tumour showed that all mice, co-administered with 4T1 and wtMSC, developed tumours within 18 days. Nevertheless, injection of 4T1 alone or in combination with MSCs \( \text{Gal-1}^{-/-} \) showed delayed tumour growth occurring between 21-32 days after initiation of the tumour. Evaluation of the animals’ survival showed good correlation with the results of tumour incidence since all mice injected with 4T1 and wtMSC died within 45 days while those obtaining 4T1 or 4T1 and MSCs \( \text{Gal-1}^{-/-} \) died between 45 and 85 days after tumour initiation. Moreover 1 and 2 animals survived over 110 days in the groups injected with 4T1 and MSCs \( \text{Gal-1}^{-/-} \) and 4T1 alone, respectively.

IV.4. MSC-induced elevation of microvessel density of primary tumours requires Gal-1 expression by MSCs

Whether Gal-1 was implicated in MSC-regulated tumour vascularisation, an \textit{in vitro} capillary assay was carried out. The absence of Gal-1 in MSCs resulted in diminished blood vessel-like structure formation when co-cultured with H5V murine endothelial cells as compared to the effect of wtMSCs. Accordingly, breast carcinoma was vascularised similarly when tumour cells were applied alone or together with MSC \( \text{Gal-1}^{-/-} \). In contrast, wtMSCs dramatically increased the vascularisation of the tumour. These results strongly indicated that Gal-1 in MSCs played an essential role in generating new capillary networks of the tumours.

IV.5. Gal-1 in MSCs is an important factor in promotion of tumour metastasis

To determine the role of Gal-1 expression in MSCs regarding the frequency of lung metastasis, the lungs of differently treated animals were macroscopically surveyed after sacrificing them. Average lung weights were around 250 mg in all experimental groups, except those from mice co-injected with 4T1 and wtMSCs which was significantly higher. Moreover, co-transplantation of wtMSCs resulted in a significant elevation of the number of lung metastatic nodules compared to that induced with MSC \( \text{Gal-1}^{-/-} \) or tumour cells alone. Decrease of Gal-1 production in siMSCs caused some but not significant change in the number of lung metastatic nodules. Accordingly, histochemical analysis of the lung tissues showed that the ratio of the metastatic area \textit{versus} the whole lung section isolated from wtMSCs co-injected animals were much higher than in lungs of animals transplanted with tumour cells alone or in combination with MSC \( \text{Gal-1}^{-/-} \). These results implied that Gal-1 expression in MSCs was critical in promoting metastasis.

IV.6. Tumorigenic effect of endogenous Gal-1 versus MSC-derived Gal-1

To find out whether endogenous Gal-1 affected tumour growth we changed breast carcinoma to melanoma model to be able to use syngeneic tumour conditions. Wild type (wt) C57BL/6 or Gal-1 knockout (Gal-1 \(-/-\)) B6.Cg-Lgals1^tm1Rob/J mice were treated with syngeneic B16F10 melanoma cells with or without wtMSCs or MSCs \( \text{Gal-1}^{-/-} \). Hardly detectable tumours were observed when Gal-1 \(-/-\) mice were injected with melanoma cells alone compared to wt animals on the 24th day of injection. Co-transplantation of wtMSCs with tumour cells accelerated tumour development in wild type mice although the enhancement was not statistically significant in contrast to growth promoting effect of wtMSCs on the growth of breast carcinoma. The difference between the two tumour types could be attributed to the extremely high aggressiveness of melanoma. More importantly wtMSCs significantly and
dramatically supported melanoma growth in Gal-1/- mice. In contrast, transplantation of tumour cells together with MSCs Gal-1/- did not promote tumour appearance until the 23rd day in Gal-1 knockout mice. The presence of Gal-1 in MSCs seemed to be essential to support tumour development in knockout mice and Gal-1 expression in tumour cells was not sufficient to entirely by-pass the endogenous Gal-1 deficiency. Accordingly, tumour growth was urged in Gal-1/- mice injected with tumour together with wtMSCs, resulting in no tumour free animals within 21 days after transplantation. Those Gal-1 knockout animals which were injected with tumour cells alone or in the presence of Gal-1 deficient MSCs showed a delayed tumour growth as the first animals developed visible tumours on the 21st and 25th day and even after 60 days of observation one and two animals remained tumour free, respectively. Co-application of wtMSCs in wt mice hardly influenced the appearance of the tumour indicating the aggressive growth of the melanoma.

V. Summary

Bone marrow derived mesenchymal stem cells (MSCs) have recently been implicated as one source of the tumour-associated stroma which plays essential role in regulating tumour progression. In spite of the intensive research, the individual factors in MSCs controlling tumour progression have not been adequately defined. In the present study we have examined the role of galectin-1 (Gal-1), a protein highly expressed in tumours with poor prognosis, in MSCs in the course of tumour development. These results confirm that galectin-1 is one of the critical factors in MSCs regulating tumour progression.

- Co-transplantation of wild type MSCs with 4T1 mouse breast carcinoma cells enhances the incidence of palpable tumours, growth, vascularisation and metastasis. It also reduces survival compared to animals treated with tumour cells alone or in combination with Gal-1 knockout MSCs.
- *In vitro* studies show that the absence of Gal-1 in MSCs does not affect the number but reduces the migration distance of migrating MSCs toward the tumour cells. Expression of Gal-1 in MSCs does not effect their localization in the tumour tissue *in vivo*.
- MSC-derived Gal-1 enhances tumour vascularisation *in vivo* and induces capillary-formation when co-cultured with H5V endothelial cells *in vitro*.
- Vital role of Gal-1 in MSCs has been further verified in Gal-1 knockout mice. By administering B16F10 melanoma cells into Gal-1 deficient animals, tumour growth is highly reduced compared to wild type animals. Nevertheless, co-injection of wild type but not Gal-1 deficient MSCs results in dramatic tumour growth and development.

VI. Acknowledgement

I would like to express my appreciation to Prof. Éva Monostori for her supervisory guidance. The members of the Lymphocyte Signal Transduction Laboratory have contributed excessively to my personal and professional time in BRC. I am especially grateful to Dr. Roberta Fajka-Boja, Éva Kriston-Pál, Dr. Ferenc Kovács-Sólyom, Dr. Ágnes Czibula, Dr. Blaskó Andrea, Julianna Novák, Enikő Szabó. They were a source of good cues and collaboration that was essential for my work. I am grateful to Dr. Ferenc Uher and his colleagues for the isolation and fluorocytometric characterization of MSCs and Prof. Krenács László, Dr. Enikő Bagdi and their staff and to Prof. Éva Fekete, Dr. Nikolett Bódi for their kind help in histology. I very much appreciate the technical assistance of Mrs. András Gercsó and Erzsébet Kusz. I would also like to acknowledge to Dr. Róbert L. Katona and Dr. Péter
Blazsó for the siRNS transfected murine MSCs as well as the help of Dr. Ferhan Ayaydin, Zsuzsanna Kószó using confocal microscopy. I thank Dr. Csaba Vizler for the 4T1 breast carcinoma cell line and Prof. Robert Kiss the B16F10 melanoma cell line. I also thank to Mária Tóth and Mrs. Szilveszter Börcsök for the preparation of photographs and figures and I am glad for the good co-operation with the Animal House governed by Erika Veres.

Publications

Gábor J. Szebeni, Éva Kriston-Pál, Péter Blazsó, Róbert L. Katona, Julianna Novák, Enikő Szabó, Ágnes Czibula, Beáta Hegyi, Ferenc Uher, László Krenács, Roberta Fajka-Boja, Gabriella Joó, Éva Monostori, Identification of galectin-1 as a critical factor in function of mesenchymal stem cell-mediated tumor promotion PLoS ONE 2012 IF(2010): 4.411 Közlésre elfogadva.

Kovács-Sólyom F, Blaskó A, Fajka-Boja R, Katona RL, Végh L, Novák J, Szebeni GJ, Krenács L, Uher F, Tubak V, Kiss R, Monostori E. Mechanism of tumour cell-induced T-cell apoptosis mediated by galectin-1. Immunology Letters (2010), Vol:127 (2): 108-118. IF(2010): 2.511

Fajka-Boja Roberta, Blaskó Andrea, Kovács-Sólyom Ferenc, Szebeni Gábor, Tóth Gábor, Monostori Éva, Co-localization of galectin-1 with GM1 ganglioside in the course of its clathrin- and raft-dependent endocytosis. Cellular and Molecular Life Sciences, (2008) 65: 2586-2593 IF(2008): 5.511

Ion G, Fajka-Boja R, Kovacs F, Szebeni G, Gombos I, Czibula A, Matko J, Monostori E.: Acid sphingomyelinase mediated release of ceramide is essential to trigger the mitochondrial pathway of apoptosis by galectin-1. Cellular Signalling, (2006) 18: 1887-1896. IF(2006): 4.887

Citable abstract

Gábor János Szebeni
The role of bone marrow derived mesenchymal stem cells and their galectin-1 expression in the progression of mouse tumors in models of 4T1 breast carcinoma and B16F10 melanoma. Acta Biologica Szegedensis Volume 54(1):70-71, 2010

R. Fajka-Boja, F. Kovács-Sólyom, R.L. Katona, G.J. Szebeni, L. Krenács, L. Végh, A. Blaskó, F. Uher, J. Novák, V. Tubak, R. Kiss, É. Monostori. Mechanism of T-cell death induced by tumor cell-derived galectin-1, that acts via direct cell-cell contact. Eur.J.Immunol, Volume 39 Issue S1, Page S195 (September 2009) IF: 5.179

Patent

Ferenc Uher, Éva Monostori, Gabriella Joó, László Krenács, Gábor Szebeni, Tamás Martinek, Vilmos Tubak, Péter Blazsó, Róbert Katona, Ferenc Kovács-Sólyom, Andrea Blaskó, András Tiborné Gercsó, Roberta Fajka-Boja
Hungarian Intellectual Property Office: P0900502, ‘Preparation for delivery of agents to solid tumors ‘ I participated in writing of the patent including the claims.
Oral presentations

1. **Szebeni Gábor János**, Kriston-Pál Éva, Blazsó Péter, Katona Róbert, Novák Julianna, Szabó Enikő, Joó Gabriella, Hegyi Beáta, Uher Ferenc, Krenács László, Fajka-Boja Roberta, Czibula Ágnes, Monostori Éva
   “Identification of galectin-1 as a critical factor in function of mesenchymal stem cell-mediated tumour promotion”, Instituto Clínico Humanitas, Milan, 02/12/2011

2. **Szebeni Gábor János**, Kriston-Pál Éva, Blazsó Péter, Katona Róbert, Novák Julianna, Szabó Enikő, Joó Gabriella, Hegyi Beáta, Uher Ferenc, Krenács László, Fajka-Boja Roberta, Czibula Ágnes, Monostori Éva
   „A Galektin-1, mint a mesenchymalis össejtek tumorfejlődésre gyakorolt hatásában azonosított új faktor”, Magyar Immunológiai Társaság XXXX. Vándorgyűlése, Kecskemét, 12-14/10/2011

3. **Gábor J. Szebeni**, Roberta Fajka-Boja, Andrea Blaskó, Éva Kriston-Pál, Ágnes Czibula, Ferenc Uher, Péter Blazsó, Róbert Katona, Gabriella Joó, László Krenács, Éva Monostori
   „Is mesenchymal stem cell - derived galectin-1 a master or staff in immunomodulation and tumor progression ?”, Straub-days, Szeged, 1-2/12/2010.

4. **Szebeni Gábor János**, Prof. Dr. Monostori Éva, Dr. Uher Ferenc, Prof. Dr. Krenács László, Dr. Joó Gabriella, Gercsó Andrásné, Dr. Fajka-Boja Roberta, Blaskó Andrea, Dr. Kovács-Sólyom Ferenc, Dr. Martinek Tamás, Dr. Tubak Vilmos
   „Anti-tumor anyagok szállítása szolid tumorokba”, A Magyar Tudomány Ünnepe, Szeged, 20/10/2010.

5. **Szebeni Gábor János**, Kriston-Pál Éva, Blazsó Péter, Katona Róbert, Joó Gabriella, Uher Ferenc, Krenács László, Blaskó Andrea, Fajka-Boja Roberta, Vizler Csaba, Monostori Éva
   „A mesenchymális össejtekben termelődő galektin-1 alapvetően szabályozza a mesenchymális össejtek tumor fejlődését serkentő hatását”, Magyar Immunológiai Társaság XXXIX. Vándorgyűlése, Szeged, 3-5/10/2010.

6. Fajka-Boja Roberta, Blaskó Andrea, Czibula Ágnes, **Szebeni Gábor János**, Blazsó Péter, Katona Róbert, Hegyi Beáta, Uher Ferenc, Monostori Éva
   „A galektin-1 termelés befolyásolja a mesenchymális össejtek limfócita proliferáció-szabályozó hatását”, Magyar Immunológiai Társaság XXXIX. Vándorgyűlése, Szeged, 3-5/10/2010

7. **Szebeni Gábor János**, Blaskó Andrea, Blazsó Péter, Katona Róbert, Joó Gabriella, Uher Ferenc, Krenács László, Fajka-Boja Roberta, Kriston-Pál Éva, Vizler Csaba, Monostori Éva
   „A csontvelői eredetű mesenchymális össejtek és az általuk termelt galektin-1 szerepe 4T1 emlő karcinóma és B16 melanóma fejlődésében”, 40. Membrán-Transzport Konferencia, Sümeg, 18-21/05/2010.

8. **Szebeni Gábor János**, Blaskó Andrea, Blazsó Péter, Katona Róbert, Joó Gabriella, Uher Ferenc, Krenács László, Fajka-Boja Roberta, Kriston-Pál Éva, Vizler Csaba, Monostori Éva
„A csontvelői eredetű mesenchymális össejtek és az általuk termelt galektin-1 szerepe a tumor fejlődésben”, Szegedi Biológus Doktorandusz Konferencia, Szeged, 17-18/05/2010.

9. **Szebeni Gábor János**
„A csontvelői eredetű mesenchymális össejtek és az általuk termelt galektin-1 szerepe a tumorfejlődésben”, Sófi József Ösztöndíj konferencia, Szeged, 24/03/2010.

10. **Szebeni Gábor János**
„A csontvelői eredetű mesenchymális össejtek hatása a tumorfejlődésre 4T1 emlő karcinóma és B16F10 melanóma egér modellekben”, Sófi József Ösztöndíj konferencia, Szeged, 25/03/2009.

11. **Gábor János Szebeni, Andrea Blaskó, Gabriella Joó, László Krenács, Csaba Vizler, Ferenc Uher Éva Monostori**
„Bone marrow derived mesenchymal stem cells influence the progression of mouse tumors in models of 4T1 breast carcinoma and B16F10 melanoma”, Straub-days, Szeged, 3/12/2008.

12. Kovács-Sólyom Ferenc, Blaskó Andrea, Katona Róbert, **Szebeni Gábor János**, Krenács László, Végh Lea, Fajka-Boja Roberta, Tubak Vilmos, Monostori Éva
„A galektin-1, mint legfőbb effektormolekula az U87-globlasztóma által indukált T sejt apoptózisba”, Magyar Immunológiai Társaság XXXVII. Vándorgyűlése, Budapest, 29-31/09/2008.

13. Fajka-Boja Roberta, Blaskó Andrea, Kovács-Sólyom Ferenc, **Szebeni Gábor János**, Tóth K. Gábor, Monostori Éva
„A galektin-1 és GM1 gangliozid kolokalizációja a klatrin- és raftfüggő endocitózis során”, Magyar Immunológiai Társaság XXXVII. Vándorgyűlése, Budapest, 29-31/09/2008.

14. Ferenc Kovács-Sólyom, Andrea Blaskó, **Gábor János Szebeni**, Vilmos Tubak, László Krenács, Roberta Fajka-Boja, Lea Vég, Éva Monostori
„The role of galectin-1 in the war of tumor cells against T cells”, Straub-napok, Szeged, 28-30/11/2007.

15. **Szebeni Gábor János**
„A humán galektin-1 által kiváltott T-sejt apoptózis molekuláris mechanizmusa”, Sófi József Ösztöndíj konferencia, Szeged, 19/04/2007.

16. **Szebeni Gábor János**
„A humán galektin-1 által kiváltott T-sejt apoptózis molekuláris mechanizmusa”, OTDK, Debrecen, 4-6/04/2007.

17. **Szebeni Gábor János**
„A humán galektin-1 által kiváltott T-sejt apoptózis molekuláris mechanizmusa”, TDK, Szeged, 1/12/2006.

18. Fajka-Boja Roberta, **Szebeni Gábor János**, Monostori Éva
„A galektin-1 nem-konvencionális endocitózisa”, Magyar Immunológiai Társaság Ifjúsági Napja, Pécs, 17/11/2006.
Conference abstract:

1. Fajka-Boja Roberta, Szebeni Gábor János, Czibula Ágnes, Hegi Beáta, Uher Ferenc, Monostori Éva
   „*Galektin-1 szerepe a mesenchymalis össejtek in vitro és in vivo immunszupresszív hatásában*” Magyar Immunológiai Társaság XXXX. Vándorgyűlése, Kecskemét, 2011. október 12-14.

2. Kriston-Pál Éva, Fajka-Boja Roberta, Czibula Ágnes, Szebeni Gábor János, Uher Ferenc, Monostori Éva
   „*Mesenchymalis össejt eredetű galektin-1 hatása az in vitro érdifferenciációra*” Magyar Immunológiai Társaság XXXX. Vándorgyűlése, Kecskemét, 2011. október 12-14.

3. Éva Kriston-Pál, Roberta Fajka-Boja, Julianna Novák, Gábor János Szebeni, Ferenc Uher, Éva Monostori
   „*Galectin-1 is required to the capillary-like structure formation in mesenchymal stem cell and endothelial cell coculture*” IMmune-related Pathologies: Understanding Leukocyte Signaling and Emerging therapies, IMPULSE, Visegrád, 2011. szeptember 3-6.

4. Fajka-Boja Roberta, Blaskó Andrea, Czibula Ágnes, Szebeni Gábor János, Blazsó Péter, Katona Róbert, Hegyi Beáta, Uher Ferenc, Monostori Éva
   „*A galektin-I funkciója a mesenchymális össejtek és a limfociták kölcsönhatásában*” IX. Magyar Genetikai Kongresszus és XVI. Sejt- és Fejlődésbiológiai Napok, Siófok, 2011. március 25-27.

5. Kriston-Pál Éva, Fajka-Boja Roberta, Novák Julianna, Szebeni Gábor János, Uher Ferenc, Monostori Éva
   „*BM-MSC eredetű galektin-1 in vitro hatása endotél sejtek proliferációjára és angiogenezisre*”, Magyar Immunológiai Társaság XXXIX. Vándorgyűlése, Szeged, 3-5/11/2010.

6. Szebeni Gábor János, Blaskó Andrea, Blazsó Péter, Katona Róbert, Joó Gabriella, Uher Ferenc, Krenács László, Fajka-Boja Roberta, Kriston-Pál Éva, Vizler Csaba, Monostori Éva
   „*A csontvelői eredetű mesenchymális össejtek és az általuk termelt galektin-1 szerepe 4T1 emlő karcinóma és B16 melanóma fejlődésében*”, 40. Membrán-Transzport Konferencia, Sümeg, 18-21/05/2010.

7. Fajka-Boja Roberta, Kovács-Sólyom Ferenc, Katona Róbert, Szebeni Gábor János, Krenács László, Végh Lea, Blaskó Andrea, Uher Ferenc, Novák Julianna, Tubak Vilmos, Robert Kiss, Monostori Éva. *Mechanism of T-cell death induced by tumor cell-derived galectin-1, that acts via direct cell-cell contact.* (Eur.J.Immunol, VOLUME 39 Issue S1, Page S195) 2nd European Congress of Immunology, ECI Berlin 13-16/09/2009.

8. Szebeni Gábor János, Blaskó Andrea, Joó Gabriella, Krenács László, Fajka-Boja Roberta, Katona Róbert, Blazsó Péter, Vizler Csaba, Uher Ferenc, Monostori Éva
9. Végh Lea, Novák Júlianna, Kovács-Sólyom Ferenc, Tubak Vilmos, Blaskó Andrea, Vácz Balázs, Szebeni Gábor János, Angyal Adrienn, Fajka-Boja Roberta, Kiss-Tóth Endre, Monostori Éva
„Galektin-1 fehérje dimerizációjának szerepe a T-sejt apoptózis kiváltásában”, Magyar Immunológiai Társaság Ifjúsági Kongresszusa, Harkány, 29-30/10/2009.

10. Blaskó A., F. Kovács-Sólyom, R. Fajka-Boja, R.L.Katona, G.J.Szebeni, L. Krenács, L.Véggh, J. Novák, V. Tubak, É. Monostori
„Mechanism of T-cell death induced by tumor cell-derived galectin-1, that acts via direct cell-cell contact”, Signals and signal processing in the immune system, Balatonöszöd, 2-6/09/2009.

11. Szebeni Gábor János, Joó Gabriella, Krenács László, Vizler Csaba, Uher Ferenc és Monostori Éva
„A csontvelői eredetű mezenchymális őssejtek hatása a tumorfejlődésre 4T1 emlő karcinóma és B16F10 melanóma modellekben”, Magyar Immunológiai Társaság XXXVII. Vándorgyűlése, Budapest, 29-31/10/2008.

12. Fajka-Boja Roberta, Blaskó Andrea, Kovács-Sólyom Ferenc, Szebeni Gábor János, Tóth K. Gábor, Monostori Éva
„A Galektin-I klatrin- és raftfüggő endocitózisa”, 38. Membrántranszport Konferencia, Sümag, 20-23/05/2008.

13. Kovács-Sólyom Ferenc, Blaskó Andrea, Katona Róbert, Szebeni Gábor János, Krenács László, Végh Lea, Fajka-Boja Roberta, Tubak Vilmos, Robert Kiss, Monostori Éva
„A galektin-I, mint legfőbb effetormolekula az U87-globlasztóma által indukált T sejt apoptózisban”, 38. Membrántranszport Konferencia, Sümag, 20-23/05/2008.

14. Fajka-Boja Roberta, Szebeni Gábor János, Monostori Éva
„A galektin-I nem-konvencionális endocitózisa”, VII. Magyar genetikai Kongresszus XIV. Sejt- és Fejlődésbiológiai Napok, Balatonfüred, 15-17/04/2007.