Is the research on RANTES/CCL5 in jawbone marrow defects science based validated?

15 scientific publications of Dr. Dr. (PhD) Johann Lechner and free PDF downloads.

Several publications by Dr. Lechner and co-authors W. Mayer and Dr. V. von Baehr have been accepted by international medical journals on the topic of "Dental Interference Fields and Systemic Diseases". The consistent theme of this publication series is research into silent chronic fatty degenerative inflammation of the jawbone (FDOJ, also known as "maxillary osteitis", "NICO"), in which the key pathogenetic element is the chemokine RANTES/CCL5 in up to 60-fold overexpression. RANTES/CCL5 is implicated in many systemic diseases - rheumatoid arthritis, breast cancer, Hashimoto's disease, melanoma, multiple sclerosis, ALS, etc. Our first laboratory detection of this inflammatory messenger in the jawbone is the contradiction-free proof of a holistic-systemic signaling effect from the jawbone with modern immunological methods. Since these articles have been peer reviewed by several experts and included in the PubMed or ScienceDirect (Elsevier) medical library for their academic rigor, these articles are to be considered accepted science and natural science undisputed part of medical progress.
The listing is chronological; always indicated is the link to the corresponding journal, followed by the link in PubMed.

1. June 2010: **European Journal of Integrative Medicine** *“Immune messengers in Neuralgia Inducing Cavitational Osteonecrosis (NICO) in jawbone and systemic interference”.* http://dx.doi.org/10.1016/j.eujim.2010.03.004

Paid download in ScienceDirect (Elsevier):
http://www.sciencedirect.com/science/article/pii/S1876382010000260

Focus and Conclusion: Pilot study of 6 cases revealing RANTES and FGF-2 out of 27 cytokines studied as singularly extremely overexpressed inflammatory messengers in chronic fatty degenerative altered jawbone (FDOJ/"NICO"/jawbone ostits).

2. April 2013: **International Journal of General Medicine: Lechner J, von Baehr V.**

"RANTES and fibroblast growth factor 2 in jawbone cavitations triggers for systemic disease"

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Link in PubMed: http://www.ncbi.nlm.nih.gov/pubmed/23637551

Abstract

Background: Jawbone cavitations (JC) are hollow dead spaces in jawbone with dying or dead bone marrow. These areas are defined as fatty degenerative osteonecrosis of jawbone or “Neuralgia Inducing Cavitational Osteonecrosis/NICO” and may produce facial pain. They have been linked with the immune system and chronic illnesses. Surgical debridement of JC is reported to lead to an improvement in immunological complaints such as rheumatic, allergic and other inflammatory diseases (ID). Little is known about the underlying cause\effect relationship.

Objectives: JC bone samples were analysed to assess the expression and quantification of immune modulators which can play a role in the pathogenesis of ID. The study supports a potential mechanism where JC is amediating link in ID.

Material and Methods: Samples of fatty softened bone taken from JC have been extracted from 31 patients. The specimens were analyzed by bead-based multiplex technology and tested for 7 immune messengers.

Results: RANTES and FGF-2 are found at high levels in the JC tested. Other cytokines could not be detected at exceeding levels.

Discussion: The study confirms that JC is able to produce inflammatory messengers, primarily RANTES secondary FGF-2. Both are implicated in many serious illnesses.The exceeding levels of RANTES /FGF-2 in JC patients with amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), rheumatic arthritis (RA) and breast cancer (BC) are compared to levels published in medical journals. Levels detected in JC are higher than in serum and cerebrospinal fluid of MS/ALS patients and four fold higher than in BC tissue.

Conclusion: The study suggests that JC might serve as a fundamental cause of ID, through RANTES/FGF-2 that they produce. Thus JC and implicated immune messengers give an integrative aspect of ID and serve as a possible cause. Removing JC may be a key to reversing ID. There is the need to raise awareness of JC throughout medicine and dentistry.

3. May 2014: **Journal of Breast Cancer: Basic and Clinical Research:** Lechner J, von Baehr V. "*Hyperactivated Signaling Pathways of Chemokine RANTES/CCL5 in Osteopathies of Jawbone in Breast Cancer Patients – Case Report and Research"*.

Free download: http://journals.sagepub.com/doi/pdf/10.4137/BCBCR.S15119

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/24899812

Over 2,000 views by April 2021.

Abstract

Background: Hollow spaces in the jawbone have been defined as fatty degenerative osteonecrosis of jawbone (FDOJ) and have been linked with a dysregulated immune system. Little is known about the underlying relationship. Objectives: Samples of FDOJ were analyzed to assess expression of cytokines which can play a role in the pathogenesis of breast cancer (MaCa). Material and Methods: Samples of FDOJ extracted from 23 patients with MaCa and 19 healthy control jawbone samples were analyzed for 7 immune messengers. Results: RANTES was found to be highly overexpressed in disease samples. No change was observed in expression levels of the other immune mediators. Discussion: This data provides a compelling confirmation that FDOJ produces high levels of RANTES, a cytokine implicated in MaCa and metastasis. Levels detected in FDOJ are five-fold higher than that previously reported for MaCa tissue suggesting its role as a cytokine source in MaCa. Conclusion: We thus hypothesize that FDOJ may serve as an expeditor of MaCa progression, through RANTES production.

4. August 2014: **Clinical, Cosmetic and Investigational Dentistry: "***Validation of dental X-ray by cytokine RANTES – comparison of X-ray findings with cytokine overexpression in jawbone".*

Free download: http://www.dovepress.com/articles.php?article_id=18049.

Over 12,888 views by July 2021.

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/25170282

Abstract

Introduction: There is a need to clarify the extent to which the most common diagnostic tool in dentistry– two-dimensional panoramic tomography (2D OPG) – is suitable for identifying fatty degenerative osteolysis in jawbone (FDOJ).

Material and methods: To obtain a qualitative assessment of edentouless jawbone sections, the results from 2D OPG with a defined X-ray density (XrDn), an expression of the cytokine RANTES, and a transalveolar ultrasound (TAU) system for measuring the jabone density will be compared.

Results: The difference in XrDn of healthy jawbone and FDOJ are minimal, whereas RANTES is up to 25-fold higher in FDOJ. In contrast to 2D-OPG TAU shows coincidental findings in FDOJ areas.

Discussion: Comparisons of the data reveal a discrepancy between the XrDn of 2D OPGs and medullary osteopathias in jawbone like FDOJ.

Conclusions: Data suggest a critical attitude towards the use of 2D-OPG as a sole imaging diagnostic tool for chronic inflammatory process in jawbone. 2D OPG is objectively not suitable for depicting FDOJ.

5. May 2015: **EPMA Journal** (European Association for Predictive, Preventive and Personalized Medicine): Lechner J, von Baehr V. *"Chemokine RANTES/CCL5 as an unknown link between wound healing in the jawbone and systemic disease: is prediction and tailored treatments in the horizon?".*2015, 6:10. doi:10.1186/s13167-015-0032-4

Free download: https://doi.org/10.1186/s13167-015-0032-4

Over 2,800 views by July 2021.

Link on PubMed: https://pubmed.ncbi.nlm.nih.gov/25987906/

Abstract

Background: This research elucidates the question of whether common and widespread dental procedures (DP) like root filling (RF) and the removal of wisdom teeth (WT) contribute to chronic inflammation in the jawbone. Dentists, in carrying out these DP, can set off defective wound healing in the jawbone in ignorance of its connection to inflammatory mediators and the possibility of it being a hidden cause of chronic systemic diseases (SYD).

Materials and Methods: We examined samples of jawbone for seven cytokines by multiplex analysis in three groups of jawbone areas. In order to clarify systemic interrelations, specimens from 16 patients were analyzed in areas of former surgery in the retromolar wisdom tooth area; specimens from 16 patients were analyzed in the jawbone, apically of teeth with RF; and specimens from 19 patients were of healthy jawbone. Each of the retromolar and the apical jawbone samples showed clinically fatty degenerated and osteonecrotic medullary changes.

Results: All fatty necrotic and osteolytic jawbone (FDOJ) samples showed RANTES and fibroblast growth factor (FGF)-2 as the only extremely overexpressed cytokines. FDOJ cohorts showed a 30-fold mean overexpression of RANTES and a 20-fold overexpressed level of FGF-2 when compared to healthy controls.

Conclusions: As RANTES is discussed in the literature as a possible contributor to inflammatory diseases, and though it might have oncogenic effects, we hypothesize that FDOJ in areas of improper and incomplete wound healing in the jawbone might act as hyperactivated signaling pathways, while serving as an unknown source of "silent inflammation". Because of the wide range of RANTES in immune diseases treating FDOJ can cover many potential prediction or prognosis of individual outcomes.

6. June 2015: Lechner J, von Baehr V. **Evidence-Based Complementary and Alternative Medicine** *"Peripheral Neuropathic Facial/Trigeminal Pain and RANTES/CCL5 in Jawbone Cavitation"*, Vol. 2015, Article ID 582520, 9 pages, 2015. doi:10.1155/2015/582520

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Table of Contents of Volume 2015: http://www.hindawi.com/journals/ecam/contents/

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/25987906

Abstract

Introduction: In this study, we attempt to elucidate the possible causative role of chronic subclinical inflammation in the jawbone of patients with atypical facial pain (AFP) and trigeminal neuralgia (TRN) in the local overexpression of the chemokine regulated on activation, normal T-cell expressed and secreted (RANTES), also known as chemokine C-C motif ligand 5 (CCL5). Neurons contain opioid receptors that transmit anti-pain reactions in the peripheral and central nervous system. Opioid-containing remedies sensitize via an agonistic contrary effect on the opioid receptors and block the conduction of pain. Proinflammatory chemokines like RANTES/CCL5 desensitize μ-opioid receptors in the periphery sensory neurons and it has been suggested that RANTES interacts with opioid receptors and modifies the nociceptive reaction.

Materials and Methods: In 15 patients with AFP/TRN, we examined fatty degenerated jawbone (FDOJ) samples for the expression of seven cytokines by multiplex analysis and compared these results with healthy jawbones.

Results: Each of these medullary jawbone samples exhibited RANTES as the only highly overexpressed cytokine. The FDOJ cohort with AFP/TRN showed a mean 30-fold overexpression of RANTES compared to healthy jawbones.

Conclusions: To the best of our knowledge, no other research has identified RANTES overexpression in silent inflamed jawbones as a possible cause for AFP/TRN. Thus, we hypothesize that the surgical clearing of FDOJ might diminish RANTES signaling pathways in neurons and contribute to resolving chronic neurological pain in AFP/TRN patients.

7. July 2017: **Journal of BIOLOGICAL REGULATORS:** J Lechner, K Huesker, V Von Baehr.“ *The impact of RANTES from jawbone on Chronic Fatigue Syndrome”.*

Abstract: www.biolifesas.org/contentsJBRHA.htm JBRHA 31, No. 2, April - June 2017

Link on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/?term=Lechner+J+CFS

Abstract

This study elucidates the question of whether chronic inflammation in the jawbone contributes to the development of Chronic Fatigue Syndrome (CFS). Fatty degenerative osteonecrosis in jawbone (FDOJ) may contribute to CFS by induction of inflammatory mediators. We examined seven cytokines by multiplex analysis in jawbone samples from two groups of patients. In order to clarify neurological interrelations, specimens from 21 CFS patients were analyzed from areas of previous surgery in the retromolar wisdom tooth area. Each of the retromolar jawbone samples showed clinically fatty degenerated and osteonecrotic medullary changes. As control healthy jawbone specimens from 19 healthy patients were analyzed. All fatty necrotic and osteolytic jawbone (FDOJ) samples showed high expression of RANTES and fibroblast growth factor (FGF)-2. FDOJ cohorts showed a 30-fold mean overexpression of RANTES and a 20-fold overexpressed level of FGF-2 when compared to healthy controls. As RANTES is discussed in the literature as a possible contributor to inflammatory diseases, we hypothesize that FDOJ in areas of improper and incomplete wound healing in the jawbone may hyperactivate signaling pathways. Constituting a hidden source of “silent inflammation” FDOJ may represent a hitherto unknown cause for the development of CFS.

8. October 2017: Lechner J, von Baehr V. **Clinical, Cosmetic and Investigational Dentistry: “**Aseptic-avascular osteonecrosis: local “silent inflammation” in the jawbone and RANTES/CCL5 overexpression.” 2017:9 99-109.

Free download: https://www.dovepress.com/articles.php?article_id=35541.

Over 7,166 views by July 2021.

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/29184447

Abstract

Of the definitions listed in the ICD-10, there are two disease descriptions that can be found together: “idiopathic aseptic bone necrosis” and “avascular bone necrosis”. The relevant literature on both conditions abbreviates both as “aseptic ischemic osteonecrosis in the

jawbone" (AIOJ). To shed light on the clinical details of this condition, osteolytic jawbone samples of 24 patients with different systemic immunological diseases were examined using four steps: presurgical dental X-ray; postsurgical histology; polymerase chain reaction DNA analysis **(**PCR DNA) of bacteria; and RANTES/CCL5 (R/C) expression. These four steps showed that neither X-ray nor histology delivered unambiguous results with respect to inflammatory processes; furthermore, the PCR results did not show evidence of any microbial load within the jaw samples. There is, however, a striking, coherent over-expression of chemokine R/C in the AIOJ samples. This study proved the aseptic existence of "silent inflammation" within the jawbone. The ICD-10 (AIOJ) definition, which is hard to interpret, can now be substantiated with clinical evidence, while the cytokine expressions described in this report can explain the systemic immunological effects observed within the group of examined patients.

9. April 2018: **International Journal of General Medicine:** *" The vitamin D receptor and the etiology of RANTES/CCL-expressive fatty-degenerative osteolysis of the jawbone: An interface between osteoimmunology and bone metabolism"*.
   Doi https://doi.org/10.2147/IJGM.S152873

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Over 8,815 views by July 2021.

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/29731660

Abstract

Background: Recent research on vitamin D indicates that our current understanding of the factors leading to chronic inflammation should be revised. One of the key mechanisms by which microbial immunosuppression occurs is the suppression of one of the most common endogenous cell nucleus receptors: the vitamin D receptor (VDR). Autoimmune diseases may be correlated with VDR deactivation (VDR-deac) which occurs when the receptor is no longer able to transcribe antimicrobial agents. Excess 1,25-dihydroxyvitamin D (1,25D) is not converted to 25-hydroxyvitamin D (25D); thus, high 1,25D levels may be accompanied by low 25D values.

Patients and methods: Since 1,25D promotes osteoclast activity and may thereby cause osteoporosis, fatty-degenerative osteolysis of the jaw (FDOJ), as described by our team,

may also be associated with VDR-deac. In 43 patients vitamin D conversion, immune system function and the quality of bone resorption and formation in the jawbone are related factors that may enhance chronic inflammatory processes. Here, we examine the relationship between immunology and bone metabolism among 43 FDOJ patients and those with immune system diseases (ISDs).

Results: We provide a link between FDOJ, RANTES/CCL5 overexpression and VDR-deac.

Conclusion: The clinical data demonstrate the interaction between VDR-deac and proinflammatory RANTES/CCL5 overexpression in FDOJ patients.

10. June 2018: **EPMA Journal/Springer:** Lechner, J., Noumbissi, S. von Baehr, V. "*Titanium implants and silent inflammation in jawbone – a critical interplay of dissolved titanium particles and cytokines TNF-a and RANTES/CCL5 on overall health?*" EPMA Journal (2018). https://doi.org/10.1007/s13167-018-0138-6

Free download: http://link.springer.com/article/10.1007/s13167-018-0138-6

Over 5,431 views by July 2021.

Link on PubMed: http://www.ncbi.nlm.nih.gov/pubmed/30174768

Abstract

Background and Introduction: *It is a well known fact that titanium particles deriving from dental titanium implants (DTI) dissolve into the surrounding bone. Although titanium (TI) is regarded as a compatible implant material, increasing concern is coming up that the dissolved titanium particles induce inflammatory reactions around the implant. Specifically, the inflammatory cytokine tumor necrosis factor alpha (TNF-*α) is expressed in the adjacent bone. The transition from TNF-α induced local inflammation following insertion of DTI surgery to a chronic stage of "silent inflammation" could be a neglected cause of unexplained medical conditions.

Material and methods: The signaling pathways involved in the induction of cytokine release were analyzed by multiplex analysis. We examined samples of jawbone (JB) for seven cytokines in two groups: Specimens from 14 patients were analyzed in areas of DTI for particle-mediated release of cytokines. Each of the adjacent to DTI tissue samples showed

clinically fatty degenerated and osteonecrotic medullary changes (FDOJ) in the JB. Specimens from 19 patients were of healthy JB. In five cases we measured the concentration of dissolved Ti particles by spectrometry**.**

Results: All DTI-FDOJ samples showed RANTES/CCL5 (R/C) as the only extremely overexpressed cytokine. DTI-FDOJ cohort showed a 30-fold mean overexpression of R/C as compared with a control cohort of 19 healthy JB samples. Concentration of dissolved Ti particles in DTI-FDOJ was 30-fold higher than an estimated maximum of 1.000 µg/kg.

Discussion: As R/C is discussed in the literature as a possible contributor to inflammatory diseases, the here presented research examines the question of whether common DTI may provoke the development of chronic inflammation in the jawbone in an impaired state of healing. Such changes in areas of the JB may lead to hyperactivated signaling pathways of TNF-a induced R/C overexpression, and result in unrecognized sources of silent inflammation. This may contribute to disease patterns like Rheumatic Arthritis, Multiple Sclerosis and other systemic-inflammatory diseases, which is widely discussed in scientific papers.

Conclusion: From a systemic perspective, we recommend that more attention be paid to the cytokine crosstalk that is provoked by dissolved Ti particles from DTI in medicine and dentistry. This may contribute to further development of personalized strategies in preventive medicine.

11. November 2018: Lechner J, Rudi T, von Baehr V. **Clinical, Cosmetic and Investigational Dentistry: "***Osteoimmunology of Tumor Necrosis Factor-alpha, Interleukin 6, and RANTES/CCL5: A Review of Known and Poorly Understood Inflammatory Patterns in Osteonecrosis*

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Over 5,859 views by July 2021.

Link on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30519117

Abstract

Background: The immune and bone systems are closely linked via cytokine crosstalk. This interdisciplinary field of research is referred to as osteoimmunology and pertains to

inflammatory and osteoarticular diseases that feature the primary expression of tumor necrosis factor-alpha (TNF-a) and interleukin (IL)-6.

Objective: Are there bone resorptive processes wherein chronic inflammatory conditions are not linked to TNF-a and IL-6 expression, but rather to the expression of other cytokines?

Materials and Methods: A comprehensive literature search was performed in PubMed Central.

Discussion: Although all diseases with cytokines involved in bone resorption (TNF-a and IL-6) are at the forefront of destructive inflammatory processes, there is one exception in the literature: fatty oxide osteoporosis/osteolysis in the jawbone (FDOJ), which is associated with significant bone softening. However, it should be noted that TNF-a and IL-6 fall below the levels found in a healthy jawbone in this condition. Another conspicuous finding is that there is a nearly 35-fold overexpression of the chemokine RANTES/CCL5 (R/C) in all FDOJ cases studied thus far in the literature.

Conclusion: FDOJ appears to represent a unique cytokine and inflammatory pattern from osteolysis in the body. R/C can be defined as the dominant carrier of a “maxillo–mandibular osteoimmunology”.

12. August 2019: Lechner J, Schulz T, von Baehr V. **EPMA Journal/Springer:** *“Immunohistological staining of unknown chemokine RANTES/CCL5 expression in jawbone marrow defects – osteoimmunology and disruption of bone remodeling in clinical case studies targeting on predictive preventive personalized medicine”.* EPMA Journal, (2019), 1-14. DOI 10.1007/s13167-019-00182-1

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Over 1,404 views by July 2021.

Link on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/31832111

Abstract

Background: Fatty-degenerative osteonecrosis in the medullary spaces of the jawbone (FDOJ) may be identified as a lesser-known source of RANTES/CCL5 (R/C) overexpression. The chemokine R/C also interferes with bone metabolism leading to osteolysis in areas affected by FDOJ. Many dental surgeries require functioning repair mechanisms, and these may be disrupted by R/C overexpression.

Objective: To clarify the way in which R/C expression from adipocytes in FDOJ causes a disturbance in osteogenesis and impacts on medullary stem cells by investigating the detection of R/C expression with immunochemical staining.

Materials and Methods: We examined the tissue samples of 449 patients with FDOJ to assess the level of the chemokine R/C using bead based Luminex® analysis. In six clinical case studies of FDOJ, we compared bone density, histological findings, R/C expression, and immunohistochemical staining.

Results: R/C is overexpressed by up to 30-fold in the 449 FDOJ cases when compared to healthy jawbone samples. The comparison of the six clinical cases consistently shows greatly reduced bone density, (i.e., osteolysis), but varies in terms of the level of agreement across the other three parameters.

Discussion: R/C from FDOJ sources may be implicated in several immune responses and considered a key pathogenetic pathway for increased adipogenesis rather than desirable osteogenesis. Adipocytes pathogenetically act via R/C expression in local FDOJ and systemically on the immune system.

Conclusion: R/C may be regarded as an important trigger for possible pathological developments in the fate of hematopoietic stem cells. FDOJ is not a rigidly uniform process but reflects changing stages of development. The absence of correlating findings should not be interpreted as a misdiagnosis. It seems appropriate to direct further research in the field of “maxillo-mandibular osteoimmunology” focusing on R/C overexpression in FDOJ areas. This may contribute to the development of personalized strategies in preventive medicine.

13. April 2021: Lechner J, Schulz T, Lejeune B, von Baehr V. Jawbone Cavitation Expressed RANTES/CCL5: Case Studies Linking Silent Inflammation in the Jawbone with Epistemology of Breast Cancer. *Breast Cancer (Dove Med Press)*. 2021; 13: 225-240; https://doi.org/10.2147/BCTT.S295488

Link on journal: https://www.dovepress.com/articles.php?article_id=63767.

Over 1,542 views by July 2021.

Link on PubMed: https://pubmed.ncbi.nlm.nih.gov/33859496/

Abstract

Background: The role of signaling pathways as part of the cell-cell communication within cancer progression becomes a crucial area. Chemokine RANTES (regulated upon activation, normal T-cell expressed and secreted), also known as the chemokine C-C motif ligand 5 (CCL5) (R/C), is a protein on which cancer research focus due to its link with aggressive cancer development.

Objective: Research on fatty-degenerative osteonecrosis in jawbone (FDOJ) shows striking overexpression of R/C in these areas. Here we try to elucidate a potential link between jawbone-derived R/C and breast cancer (BC) and compare these findings by immunohistochemical staining.

Methods: 39 FDOJ samples extracted from 39 BC patients and samples from 19 healthy control were analyzed for R/C expression using beadbased Luminex® analysis. R/C levels from 5 BC patients were measured in serum before and after FDOJ surgery. Bone density, histology, R/C expression, and immunohistochemistry were analysed in 4 clinical case studies. The R/C staining of two FDOJ BC patients is compared with the immunohistochemical staining of BC cell preparations.

Results: A high overexpression of R/C was seen in all FDOJ samples. R/C levels in serum were statistically downregulated after FDOJ surgery (p=0,0241).

Discussion: R/C induced "silent inflammation" in BC are widely discussed in scientific papers along with R/C triggering of different signaling pathways, which might be a key point in the development of BC.

Conclusion: Hypothesis that FDOJ may serve as a trigger of BC progression through R/C overexpression was set by the authors, who thus inspire clinicians to make aware of FDOJ throughout the dental and medical community in BC cases.

14. April 2021: Lechner J, Schmidt M, von Baehr V, Schick F. Undetected Jawbone Marrow Defects as Inflammatory and Degenerative Signaling Pathways: Chemokine RANTES/CCL5 as a Possible Link Between the Jawbone and Systemic Interactions? *J Inflamm Res*. 2021; 14: 1603-1612; https://doi.org/10.2147/JIR.S307635

Link on journal: https://www.dovepress.com/articles.php?article_id=64152

Over 1,210 views by July 2021.

Link on PubMed: https://pubmed.ncbi.nlm.nih.gov/33911892/

Abstract

Background: Cytokines, especially chemokines, are of increasing interest in immunology. This study characterizes the little-known phenomenon of “bone marrow defects of the jawbone” (BMDJ) with known overexpression of the chemokine RANTES/CCL5 (R/C).

Purpose: Our investigation clarifies why BMDJ and the intensity of local R/C overexpression are challenging to detect, as examined in patients with seven different systemic immunological diseases. Specifically, we investigate whether R/C overexpression is specific to certain disease groups or if it represents a type of signal disruption found in all systemic immunological diseases.

Patients and methods: In a total of 301 patients, BMDJ was surgically repaired during clinical practice to reduce “silent inflammation” associated with the presence of jaw-related pathologies. In each case of BMDJ, bone density was measured preoperatively (in Hounsfield Units [HU]), while R/C expression was measured postoperatively. Each of the 301 patients suffered from allergies, atypical facial and trigeminal pain, or were diagnosed with neurodegenerative diseases, tumors, rheumatism, chronic fatigue syndrome, or parasympathetic disorders.

Results: In all BMDJ cases, strongly negative HU values indicated decreased bone density or osteolysis. Consistently, all cases of BMDJ showed elevated R/C expression. These findings were consistently observed in every disease group.

Discussion: BMDJ was confirmed in all patients, as verified by the HU measurements and laboratory results related to R/C expression. The hypothesis that a specific subset of the seven disease groups could be distinguished either based on the increased presence of BMDJ and by the overexpression of R/C could not be confirmed. A brief literature review confirms the importance of R/C in the etiology of each of the seven disease groups.

Conclusion: In this research, the crucial role played by BMDJ and the chemokine R/C in inflammatory and immune diseases is discussed for seven groups of patients. Each specific immune disease can be influenced or propelled by BMDJ-derived R/C inflammatory signaling pathways.

15. July 2021: Lechner J, von Baehr V, Schick F. RANTES/CCL5 Signaling from Jawbone Cavitations to Epistemology of Multiple Sclerosis – Research and Case Studies. *Degener Neurol Neuromuscul Dis*. 2021; 11: 41-50. https://doi.org/10.2147/DNND.S315321.

Link to paper in journal: https://www.dovepress.com/articles.php?article_id=66565

Over 470 views by July 2021.

Link to paper on PubMed: https://pubmed.ncbi.nlm.nih.gov/34262389/

Abstract

Background: The role played by signaling pathways in the cell–cell communication associated with multiple sclerosis (MS) progression has become a critical area in research. Chemokine RANTES (regulated upon activation, normal T-cell expressed and secreted), also named chemokine C-C motif ligand 5 (CCL5; R/C), is a protein that has been investigated in neuroinflammatory research due to its link to MS development.

Objective: Research on bone marrow defects in the jawbone (BMDJ), which morphologically present as fatty-degenerative osteonecrosis of the jawbone (FDOJ), present overexpression of R/C signaling in affected areas. Here, we try to elucidate the potential link between jawbone-derived R/C and MS.

Methods: Seventeen BMDJ/FDOJ samples extracted from 17 MS patients, as well as samples from 19 healthy controls, were analyzed for R/C expression using beadbased Luminex® analysis. The serum R/C levels from 10 MS patients were examined. Further, bone density, histology, and R/C expression were analyzed in two clinical case studies.
Results: High R/C overexpression was found in all BMDJ/FDOJ samples obtained from the MS group. Serum R/C levels were also upregulated in the MS group. R/C serum levels in the MS cohort were higher than in the healthy controls. In contrast, the histology of BMDJ/FDOJ samples showed no inflammatory cells.

Discussion: R/C-induced "silent inflammation" in MS is widely discussed in the scientific literature, along with R/C triggering of inflammation in the central nervous system, which might be key in the development of MS.

Conclusion: The authors suspect that BMDJ/FDOJ may serve as a trigger of MS progression via R/C overexpression. As such, the dental and medical communities should be made aware of BMDJ/FDOJ in cases of MS.