Congress Review

Review of European Academy of Allergy and Clinical Immunology (EAACI) Hybrid Congress 2021

Location: Kraków, Poland and Madrid, Spain

Date: 10th–12th July 2021

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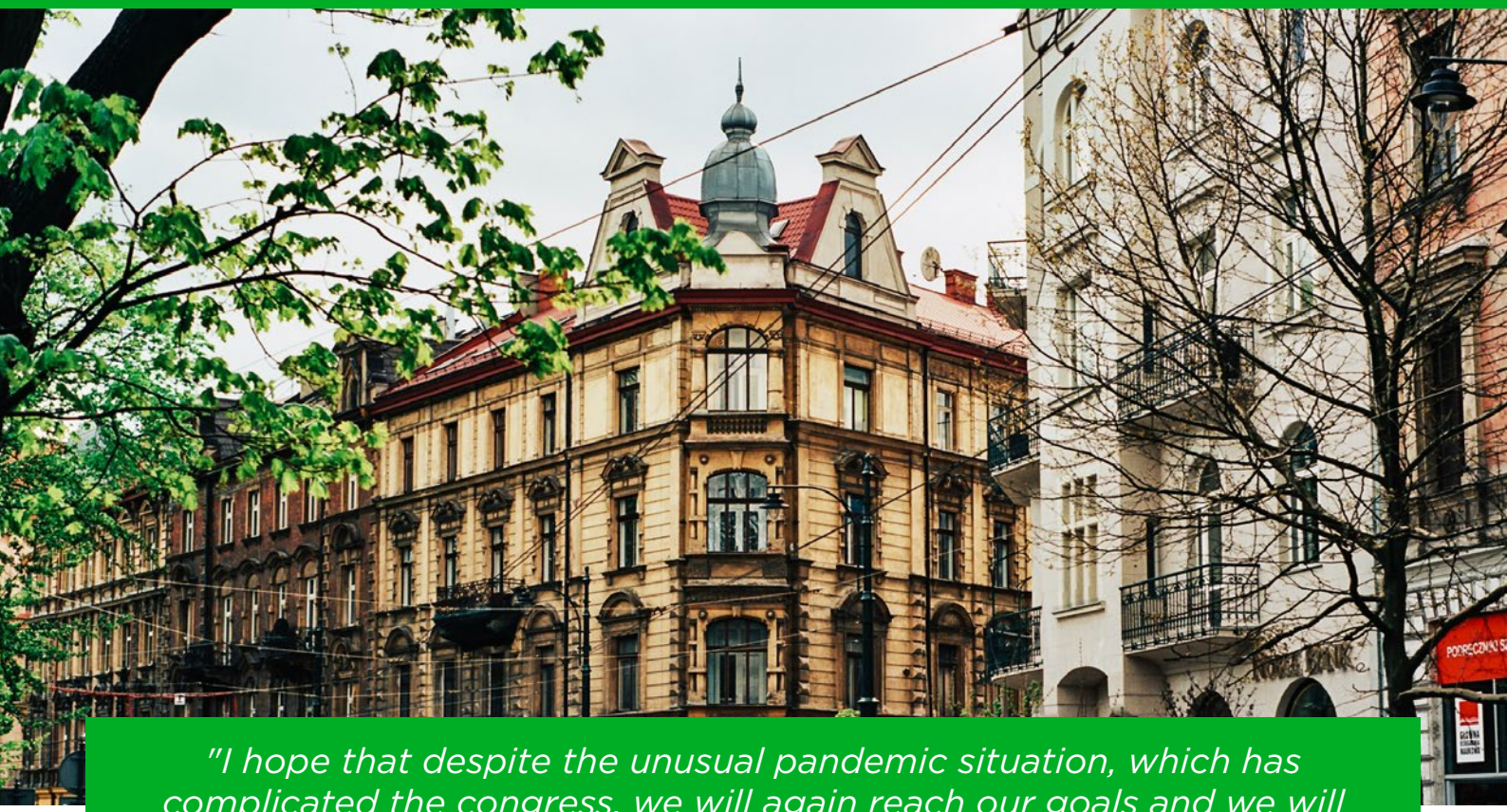
A PIONEERING format was adopted for this year's European Academy of Allergy and Clinical Immunology (EAACI) Congress, as a hybrid model was adopted for the congress to enable both digital and in-person attendance for delegates. The congress, which was attended by more than 1,000 delegates on-site and 6,500 delegates online, was co-organised by the Spanish Local Organising Committee and the Polish Society of Allergology, with the in-person sessions taking place in the historical city of Kraków, Poland, 10th–12th July 2021, under special precautions imposed by COVID-19. In his introductory remarks from Krakow, Marek Jutel, President of EAACI, hailed this new format as a great success. Joakim Sastre, Chair of the Spanish Local Organising Committee, highlighted: "This type of hybrid congress breaks into a new era of how to celebrate congresses, at least in the near future."

With close to 1,300 research abstracts submitted to the congress, the abstract themes centred around the patient, allergy, and COVID-19. This year's congress saw a total of six plenary symposia, nine further symposia, and 23 hybrid interactive workshops, in which the speakers addressed some frequently asked questions on relevant topics. For the first time, the congress also hosted a total of three World Leadership Dialogues, which are high-level sessions aiming to present the high-calibre science by top researchers on key topics that aim to complement the plenary themes and sessions. The overarching theme for this year's congress centred around harmonising research with patient care in allergy, asthma, and clinical immunology. The patient was at the forefront of research presented in the congress, with COVID-19 and food allergy being dominating themes.

In his introductory comments, Marek Kulus, Chair of the Polish Organising Committee, commemorated Marek Kowalski, a former President of the Polish Society of Allergiology and Treasurer of EAACI, who sadly passed away 3 weeks prior to the congress. "I hope that despite the unusual



"I hope that despite the unusual pandemic situation, which has complicated the congress, we will again reach our goals and we will not allow this to slow the development of allergology"

pandemic situation, which has complicated the congress, we will again reach our goals and we will not allow this to slow the development of allergology," Kulus commented.

In his speech, Santiago Quirce, a Chair of the Congress, elaborated on the motto of this year's congress stating that "it is particularly important to harmonise and integrate clinical practice with research focussed on the field, with the aim of achieving a solid scientific purpose and developing a practical and generalised framework that allows to implement allergy practice under optimal conditions." Quirce stated that it is important to adapt to the great challenges that are faced in the current world, and to better understand the role of allergy and immunology in the future that we are going to build together.

The awards ceremony saw a number of researchers receiving prestigious awards: Isabella Annesi-Maesano, INSERM Research Director, Université de Montpellier, France, was the recipient of the Clemens von Pirquet Award for Clinical Research 2021. Ewa Nizankowska, Jagiellonian University Medical College, Kraków, Poland, received the Daniel Bovet Award for Treatment and Prevention 2021. The Paul Ehrlich Award for Experimental Research went to Heim Breiteneder, University of Vienna, Austria, for his research in the field of Molecular Allergology. Stefan Vieths, Johann Wolfgang Goethe-Universität Frankfurt am Main, Germany, was the winner of the Charles Blackley Award for the Promotion of the Specialty in Europe. Oscar Palomares, Complutense University of Madrid, Spain, was the recipient of the PhARF Award, and María del Mar del Pinos Yanes was the recipient of Allergopharma Award. Jean Bousquiet, Charité– Universitätsmedizin Berlin, Germany, and Mübeccel Akdis, the Swiss Institute of Allergy and Asthma Research, Davos, Switzerland, were the recipients of the EAACI Fellow Award. Finally, Graham Roberts, University of Southampton, UK, and Stephen Durham, Imperial College London, UK, were awarded the Clinical and Research Fellow awards, respectively.

Looking to the year ahead in preparation for EAACI 2022, the organising committee are yet to finalise their plans on the location and the format of next year's congress. In light of the everchanging situation with COVID-19, this is not surprising. If anything, the EAACI Hybrid 2021 pioneered a highly successful format that can be implemented again if necessary. ■

EAACI 2021 REVIEWED →

Flare-up Phenomenon of the SARS-CoV-2 Vaccine Following Epicutaneous Testing with Polyethylene Glycol

AT THIS YEAR'S EAACI Hybrid Congress, 10th-12th July 2021, Inés Torrado Español, Guadalajara University Hospital, Spain, and collaborators presented the case of a 41-year-old female diagnosed with β-lactam hypersensitivity who was referred to their allergy department in 2005 because a large local reaction (from elbow to shoulder) developed within several hours of receiving the influenza vaccine. The reaction disappeared after 1 week, following treatment with oral and topical corticosteroids. As a result of the current COVID-19 pandemic, the patient enquired about the possibility of having the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine administered.

The authors performed skin prick and intradermal (ID) tests with the available influenza vaccine as well as prick and ID (using dilutions of 1:100, 1:10, and 1:1) tests with the available SARS-CoV-2 vaccine. Tests with the influenza vaccine were negative. A positive 1:10 ID test was recorded with the SARS-CoV-2 vaccine. In addition, the 1:1 ID test was also found to be positive; however, later studies indicated that this concentration seemed to be irritating and therefore it was not taken into account.

Several influenza vaccines commercialised in Spain are known to contain polysorbate 80, which has shown cross-reactivity with polyethylene glycol, a preservative used in the latest SARS-CoV-2 vaccine. For this reason, the researchers conducted epicutaneous tests with both polysorbate 80 and polyethylene glycol 400 7 days after neutralisation of the first tests. Although polysorbate 80 was negative, polyethylene glycol 400 was shown to be positive 96 hours later. Moreover, it reactivated both the 1:10 and 1:1 ID tests of the SARS-CoV-2 vaccine.

In summary, the authors highlighted a flare-up phenomenon of ID tests to the SARS-CoV-2 vaccine after an epicutaneous test with a low-molecular-weight grade of polyethylene glycol. This is notable for potentially being the first documented case report of its type, involving polyethylene glycol and the SARS-CoV-2 vaccine. ■

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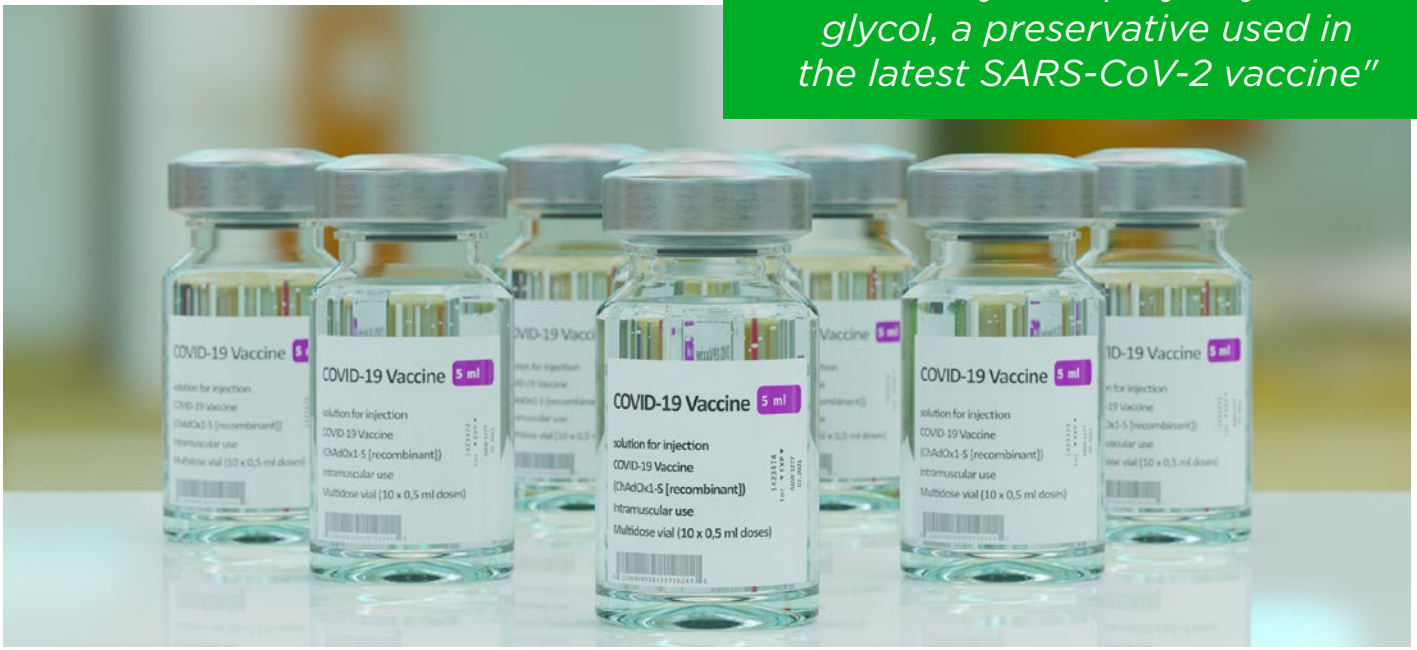

Reduced Allergenic Potentialof Birch Pollen with Vitamin D3

BIRCH trees produce birch pollen, which is responsible for hay fever in 25% of sufferers. Birch pollen can travel long distances in the wind, and people can experience allergic reactions even if they are nowhere near this silver-barked tree. Bet v 1 is a major type of birch pollen that can bind small ligands such as lipocalin to its intramolecular pocket. In a previous study, researchers from the University of Vienna, Austria discovered Vitamin D3 (VD3) could bind to this pocket. This discovery led the scientists to investigate whether the binding of VD3 affects the ability of Bet v 1 to cause an allergic reaction.

"The results showed a significant decrease in the cytokines levels of IFNγ and IL-10 in VD3 loaded allergen compared with the empty allergen."

To begin with, *in silico* docking analysis predicted the high binding affinity of VD3 to Bet v 1. This result was confirmed by *in vitro* ANS binding assay. Researchers used donated peripheral blood mononuclear cells from individuals allergic to birch pollen to determine various immune-related cellular processes such as mast cell release, production of cytokines, IgE binding, and CD-marker expression with empty allergen without VD3 and VD3 loaded allergen.

The results showed a significant decrease in the cytokines levels of IFNγ and IL-10 in VD3 loaded allergen compared with the empty allergen. The allergen loaded with VD3 decreased the expression of co-stimulatory molecules HLA-DR+ and CD68+ on CD14+ monocytes. Further to this, VD3 loaded allergen showed a significant decrease of T-cells expressing the Th-2 marker, specifically in the CD3+CD4+ cells. However, regulatory T-cells were the same in empty allergen and VC3 loaded allergen.

The researchers also observed a reduction in other cells such as CD19+ and mediator release from primary mast cells in VC3 loaded allergen. Interestingly, ELISA showed IgE binding was significantly reduced in VD3 loaded allergen compared to the empty allergen. From the *in silico* structural analyses, the scientists inferred that the binding of VD3 to the allergen could be interfering with the IgE binding site in Bet v 1.

Overall, the scientists concluded that the allergen loaded with VD3 had immunomodulatory properties. Additionally, from the decrease of cytokine levels and other immune cells, the data suggests that VD3 binding reduces the ability of Bet v 1 to cause an allergic reaction. Future studies could involve testing the efficacy of VD3 in treating birch pollen allergies in human clinical trials. ■

Pronounced Type 2 Immune Response in Nasal Polyps Cells

CHRONIC rhinosinusitis with nasal polyps (CRSwNP) is a painful condition characterised by inflammation and large non-cancerous growths inside the nasal cavity or sinuses. One out of 10 patients with CRSwNP have asthma and intolerance to non-steroidal anti-inflammatory (NSAID) drugs; this sub-type is called NSAID-exacerbated respiratory disease (N-ERD). Although there are similarities between the nasal polyps in N-ERD and CRSwNP, a detailed phenotypic characterisation of the cells involved is yet to differentiate the two conditions.

"Intriguingly, the expression of genes linked to a type 2 response, TSLP and POSTN, was distinctly elevated in N-ERD. "

To discriminate between N-ERD and CRSwNP, the authors of a new study conducted a transcriptomic analysis of epithelial cells and leukocyte subsets found in both conditions. Firstly, the scientists performed flow cytometric sorting followed by single-cell RNA sequencing of the nasal polyp tissue in N-ERD and CRSwNP. Finally, the scientists assessed the cytokines from the nasal secretions and serum of patients using a multiplex ELISA-based approach.

The results from the flow cytometric sorting showed that in N-ERD and CRSwNP, CD8+ and CD4+ T-cells formed the largest cell clusters. Other large cell clusters included NK cells, mast cells and macrophages. When analysing gene expression, scientists discovered that there were only minor differences in T-cell clusters between the two conditions. On the other hand, there was higher gene expression of most cell types in N-ERD, namely EGRF-ligand AREG and cytokines TGFB and NEAT1. Intriguingly, the expression of genes linked to a type 2 response, TSLP and POSTN, was distinctly elevated in N-ERD. Further to this, there was also an increase in IL13, IL17RB and HPGD expression in most mast cell clusters in N-ERD. Lastly, cytokine analysis showed significantly higher 1L-5 and IL-13 in N-ERD compared to CRSwNP.

In conclusion, the analysis of epithelial and mast cells showed there was a higher expression of genes involved in Type 2 immune response in patients with N-ERD. The findings suggest that mast cells are a key player in the development of N-ERD. Moving forward, scientists could explore the possibility of targeting the elevated genes or mast cells found in N-ERD to treat this painful condition. ■

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Cytokine IL-33 as a Potential Therapeutic Target in Asthma

DEFINING the relationship between serum IL-33 and the severity of asthma symptoms could reveal IL-33 as a potential therapeutic target in asthma treatment. This relationship was explored in research carried out at Nuevo Hospital San Rogue in Córdoba, Argentina, shared at EAACI 2021 and in a press release dated 13th July 2021. IL-33 is an inflammatory cytokine which acts upon several immune cells, including eosinophils, through its receptor sST2. For this reason, IL-33 has recently become a focus for research in asthma and allergic disease.

The study recruited 129 patients with asthma and divided into three severity groups, mild (n=25), moderate (n=69), and severe (n=35) along with 59 healthy controls. All patients had their blood levels of IL-33, sST2, IgE, and Eosinophils measured. A skin prick test was also carried out to establish responses to air antigens relevant to the region (Argentina). A multivariant analysis was used to compare results from the serum tests to asthma severity and prick tests. Significance was considered ($p<0.05$). This multivariant analysis research was presented at the EAACI Hybrid Congress which took place on the 10th–12th July 2021.

When serum levels were compared between patients with asthma and controls, a significant increase for all the measured elements was demonstrated in the asthmatic group: IL-33 ($p=0.0021$), sST2 ($p<0.0001$), IgE ($p<0.0001$), and eosinophils ($p<0.0001$). The prick test was positive for 92 cases of the asthmatic group and negative for 32. The multivariant analysis showed a strong correlation of 92% between the assessed components.

The results demonstrated a dramatic increase in levels of IL-33 and its receptor sST2 in patients with asthma over the control group. The multivariant analysis further suggests that increasing levels of IL-33 in the serum are linked to worsening severity of symptoms. This supports the hypothesis that IL-33 is a strong contender for a therapeutic target in asthma research and treatment. ■

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Could IL-3 Treatment Improve Allergic Asthma through ILC2 Regulation?

PROMISING developments have emerged linking recombinant IL-3 (rIL-3) treatment and improved lung function in allergic asthma. This research was prompted following recent reports of IL-3 downregulation being associated with severe allergic asthma in children. The experiment carried out by scientists in the Department of Molecular Pneumology at Friedrich-Alexander-Universität (FAU) used an Ovalbumin (OVA)-induced murine model and offers important data regarding the role of IL-3 in allergic asthma treatment through innate lymphoid cell (ILC) regulation. These findings were presented at EAACI, which took place from 10th–12th July 2021.

Cases of allergic asthma see symptoms including induced airway inflammation, airway hyperresponsiveness, mucus production and airway remodelling, all of which have been associated with abnormal differentiation of cytokine-producing Th2 cells. ST2+-ILC2 cells, which produce a variety of Th2 cytokines, have been identified to play a part in allergic asthma. The IL-3 cytokine is known to facilitate specific immune cell differentiation and survival; however, its role on ILC2 in asthma is lacking, further warranting the research carried out at FAU.

The FAU experimental murine model treated the asthmatic mice both with and without low and high intranasal doses of rIL-3 *in vivo* and expanded lung ILC2s using *in vitro* methods. This took place over a period of 5 days and results were analysed using flow cytometry. Increased lung inflammation was observed which correlated with the presence of IL-5, granulocyte-macrophage colony-stimulating factor (GM-CSF), and IL-13 cytokines in lung cells of IL-3-deficient mice. The results also demonstrated an increase in ST2hi memory-type Th2+, killer cell lectin-like receptor-G+, Thy-1+-gated (ST2hi+KLRG+Thy1+gated) on lineage-marked (Lin)-ILC2s in OVA-induced asthmatic mice, however these observations lacked in OVA-mice treated with rIL-3 *in vivo*. Mice treated with rIL-3 also saw reduced airway hyper-responsiveness and serum IgE. These data suggest that IL-3 plays an important role in the resolution of allergic asthma by regulating ILC2 and therefore opens new strategies for immunotherapy of this disease. ■

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Endothelial Cells Pattern Profile Altered by the *in vitro* Contact of Acute Anaphylaxis Serum

ANAPHYLACTIC reaction has a rapid onset and is life-threatening especially due its pathophysiology within the cardiovascular system. Previous studies have shown that patients who have undergone an anaphylactic reaction have differential extracellular vesicle (EV) protein pattern profile, however additional molecular research is required to understand the association of endothelial cells (EC) and EV release during anaphylactic reactions. A new study presented at the EAACI Congress 2021 that took place on 10th–12th July by Sergio Fernandez-Bravo, Fundación Jiménez Díaz University Hospital Health Research Institute, Madrid, Spain, aimed to look into the EC metabolic profile.

"The results of the immunoblotting assays, after 2 hours, showed an increase of EVs syntenin-1 of A-EVs-ECs supernatants compared to B-EVs-ECs supernatants"

The researchers collected plasma samples from patients during acute phase (A) anaphylaxis reaction and at the baseline (B) following recovery and purified via ultracentrifugation. ECs incubated with A and B-EVs-free plasma samples were collected for 2 and 24 hours, using an *in vitro* system. An immunoblotting technique was used to identify EVs' syntenin-1 protein expression from the EC supernatants. Platelet-activating factors and histamine were utilised as positive controls. Additionally, the EC lysates that had been stimulated for 2 hours by the collected A and B samples were quantified using liquid chromatography coupled to mass spectrometry. A multivariate model of partial least squares discriminant analysis was used to assess the differences between A and B samples.

The results of the immunoblotting assays, after 2 hours, showed an increase of EVs syntenin-1 of A-EVs-ECs supernatants compared to B-EVs-ECs supernatants. The stimulation of platelet-activating factors and histamine also elevated the expression syntenin-1 EVs-ECs for the initial 2 hours, however after 24 hours no further substantial changes were observed. Interestingly, the metabolic profile for the studied samples was only from ECs which consisted of 687 compounds. Further statistical analysis noted that 77 metabolites were identified between ECs incubated with both A and B samples. In conclusion, there is a clear increase of the EVs release and change in metabolic pattern profile in endothelial cells A samples compared to B samples. ■

New Research Could Revolutionise Immunotherapy in Canines

IMMUNOTHERAPY has gained momentum as an option for cancer treatment in humans. Previous studies have demonstrated that monoclonal antibodies (mAbs) are effective in blocking checkpoint inhibitors like PD-1 and PD-L1 which are anti-cancer therapeutics. Although the advancements in applications for immunotherapy in humans are evolving, its is unfortunate that dog anti-immunotherapy is lagging. A study presented at the EAACI Congress that took place on 10th–12th July 2021 by Rodolfo Bianchini, University of Vienna, Austria aimed to address this limitation.

A pairwise sequence alignment with EMBOSS Needle webtool was used to identify the similarities between human and dog PD-1 and PD-L1 protein sequences. Additionally, the binding effectiveness of the human antigen presenting cells therapeutic mAbs targeting both PD-1; pembrolizumab, nivolumab, and cemiplimab, and PD-L1; atezolizumab, avelumab, and durvalumab, was evaluated on the on the canine macrophage-like cell line DH82 by flow cytometry. THP1 and U937 the human monocytic cell lines were included as controls. A ligation-independent cloning technique was the used to produce canine models, with the highest binding efficiency, of the human anti-PD-1 and anti-PD-L1 mAbs.

"This study discloses a novel approach in the production of anti-PD-1 and anti-PD-L1 mAbs in canines and further research may lead to dog anti-cancer therapies using the checkpoint inhibitors."

The results from the pairwise sequence alignment revealed a similarity of 66.2% between human-PD-1; Uniprot Q15116 and canine-PD-1; A0A024FCJ9. In addition, a similarity percentage of 75.7% between human-PD-L1; Uniprot Q9NZQ7 and canine-PD-L1; EZRKZ5. The human therapeutic mAbs pembrolizumab and atezolizumab also revealed a high binding capability to the DH82 canine macrophage cell line. Using the ligation-independent cloning the researchers generated canine mAbs to create a pVitro1 cassette for fast genetic recombination of various human heavy and light chain sequences with canine IgG1 or IgG4 heavy and k light chain sequences, acquired from the international Immunogenetics information system (IMGT) database. This study discloses a novel approach in the production of anti-PD-1 and anti-PD-L1 mAbs in canines and further research may lead to dog anti-cancer therapies using the checkpoint inhibitors. ■

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