Pontificia Universidad Javeriana
Facultad de Ciencias

Grupo de Inmunobiología y Biología Celular
Programa GAT

Simposio de Investigación en Cáncer GAT

Resúmenes de las presentaciones

Edificio 95 - Manuel Briceño Jáuregui S.J

Auditorio Jaime Hoyos S.J.

Bogotá D.C. Agosto 17, 18 y 19 de 2022

Towards the personalized management of breast cancer patients

Name of the speaker:
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Abstract
Experimental evidence in cancer animal models and clinical trials results suggest that some neoadjuvant chemotherapy or radiotherapy regimens stimulate the immune system. Doxorubicin is a chemotherapeutic agent widely studied for its ability to induce a type of cell death that favors the cross-presentation of tumor antigens by dendritic cells (DCs) important for tumor immunity. Neoadjuvant treatment with Doxorubicin and Cyclophosphamide (A/C regime) is widely used in patients with breast cancer and its immunostimulatory effect deserves to be analyzed. In our work, the use of Flow Cytometry has allowed us to establish, in the blood of patients with breast cancer treated with A/C, some correlations between the clinical response of patients treated with A/C and phenotypes of leukocyte response both in vitro and ex vivo. On the other hand, whereas autologous dendritic cells (DC) are helpful as a natural vaccine adjuvant for cancer immunotherapy, the omics sciences allow the study of tumor immune infiltrate as a prognostic factor and the identification of tumor neoantigens useful for the design of personalized cancer vaccines. In this work we present some results that suggest the usefulness of (i) autologous DCs administered to patients with breast cancer treated with A/C to evidence the value of tumors as cryptic vaccines; (ii) the study of the tumor exome and transcriptome to monitor the immune infiltrate of the tumor in response to treatment, and (iii) the tumor neoantigens formulated in autologous DCs as a vaccine for breast cancer immunotherapy. Altogether, our results suggest that the combined use of flow cytometry, the analysis of the immune infiltrate of the tumor, and neoantigen-based vaccines formulated in autologous DCs as adjuvants, might allow in the near future the personalized management of breast cancer patients treated with neoadjuvant chemotherapy.

The breast cancer immune microenvironment is modified by neoadjuvant chemotherapy

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Name of the speaker:
Claudia Patricia Urueña Pinzón

Introduction:
Neoadjuvant chemotherapy (NAT) in breast cancer (BC) has been used to reduce tumor burden prior to surgery. However, the impact on prognosis depends on the establishment of Pathological Complete Response (pCR), which is influenced by tumor-infiltrating lymphocyte levels and the activation of the antitumor immune response. Nonetheless, NAT can affect immune infiltration and the quality of the response.

Aim:
evaluated the effect of NAT on the Tumor microenvironment (TME) by analyzing the immune cell populations present in the tumor as well as the diversity of the T cell response in blood and tumor before and after NAT in BC patients.

Experimental Design:
Peripheral blood and tissue samples from BC patients were collected before and after NAT, as well as tissue from healthy donors. Immune subpopulations were evaluated by immunohistochemistry and flow cytometry. Additionally, clonal expansion and T lymphocyte diversity were analyzed in some patients by TCR sequencing.

Results:
Here, we showed that NAT induces dynamic changes in the TME. After NAT, an increase of regulatory T cells and a decrease of $CD8^+$ T cells was found in tumor, correlated with the presence of metastatic cells in lymph nodes. In addition, an increase of polymorphonuclear myeloid-derived suppressor like cells was found in luminal patients post-NAT. pCR patients showed a balance between the immune populations, while non-pCR patients presented an inverse relationship in the frequency of $CD68^+$ *versus* $CD3^+$, $CD8^+$, and $CD20^+$ cells. Moreover,

activated T cells were found in peripheral blood, as well as an increase in T cell clonality with a lower diversity post-NAT.

Conclusions:
Overall, these results shown that NAT induces an activation of immune response, however, a balance in the TME seems to be related to a better antigenic presentation and therefore a better response to treatment.

DAMPs expression in acute myeloid leukemia cell lines treated with plant extracts P2Et and Anamú-SC their relationship with energetic metabolism and implications in phenotype and functionality of antigen presenting cells

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Name of the speaker:
María Paula Aulestia Vacca.

The evidence that under certain conditions, treatment with chemotherapy stimulates the immune system has been accumulating, specifically some chemotherapeutic agents used for Acute myeloid leukemia (AML) treatment, namely Daunorubicin and Etoposide induce immunogenic cell death (ICD) which promotes the release of DAMPs and the activation of the immune system against leukemia cells. AML is a heterogenous disease, including immune and metabolic differences that have repercussions in the prognosis and response to treatment in the patients. It has been demonstrated that in some cases the catastrophic death caused by chemotherapeutics alone might result in a more suppressive response instead of the desired effector function of the immune system.

Plant extracts as a multi-target strategy might sensitize the leukemia cells to death induced by the chemotherapy, additionally, it has been demonstrated that the treatment with some of them might result in the induction of ICD markers and/or the modulation of the energetic metabolism. Thus, the aim of this study is to determine the DAMPs expression after the treatment with P2Et and Anamú-SC, their relationship with energetic metabolism and the implications of those two in the phenotype and functionality of monocyte derived dendritic cells.

To achieve this, two cell lines (U937 and K562) where evaluated for death induction between energetic modulators (2-DG and Rotenone), and plant extracts P2Et and Anamú-SC with the chemotherapeutic daunorubicin to determine if they have antagonism, additive or synergistic effect by an MTT assay. The induction of ICD after the treatment alone was evaluated by the detection of translocated calreticulin (CRT) to cell membrane, and ATP in culture supernatant. Finally, a co-culture is performed with the leukemia cells treated and monocyte derived dendritic cells and the changes in the immunophenotype is evaluated.

Both metabolic modulators and plant extracts have synergy combinations with daunorubicin, and overall additive effect. Treatment with P2Et and Anamú-SC induces translocation of CRT at similar levels to the ones generated by daunorrubicin. The co-culture between AML treated cells and iCDs induces maturation and differences in immunosuppressive enzymes expression.

The use of plant extracts as co-adjuvants with classical chemotherapeutic agents can favor the elimination of tumor cells as they not only induce ICD, but they modulate energetic metabolism that might promote the development of an effector immune response.

Tumor mitochondrial metabolism modulation impact on plant extracts antitumoral activity

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Introduction

Plant extracts derived from *Caesalpnia spinosa* (P2Et) and *Petiveria alliacea* (Anamu SC) have shown antitumor activities in breast cancer mouse model, the first one has a clear role in immunogenicity and the second one modulates tumor metabolism

Aim

Metabolic differences in tumor cells such as glycolytic or OXPHOS cells are relevant on cancer pathogenesis, we evaluate the relationship of metabolic features with tumorigenic traits and immunogenicity modulated by plant extracts.

Experimental design

4T1 clones with Hexokinase 2 (*Hk-2*) and C1qbp knockdown, proteins associated with glycolytic and OXPHOS metabolism respectively, they were treated with P2Et and Anamu SC to analyze glucose uptake (GU), ROS, and ATP production, as well as migration and DAMPs expression.

Results

Breast cancer cell clone *Hk-2* showed an increase in sensitive to Anamu SC treatment, with a huge decrease in GU and ATP production with a ROS production augmentation and less wound healing closure. Meanwhile, P2Et treatment in the same clone showed a clear ROS production decreased with no changes in GU, ATP production and wound healing closure, however it increased the expression of DAMPs as calreticulin, HSP70 and HSP90. In C1qbp deficient clone a similar sensitive was observed in P2Et and SC treatment compared to 4T1 *wild type* cells; the P2Et treatment showed an mild decrease in ATP production and ROS decreased with minimal differences in GU and wound healing closure and it has not effect on DAMPs expression. Anamu SC treatment in this clone showed less GU and ATP production than WT cells with a reduction in wound healing closure assay.

Conclusions

These results partially show that glycolysis metabolism modulation treated with P2Et and SC present a major impact on tumor metabolic features as well on DAMPs expression, however, it is necessary to extend these analyzes from these mechanistic models.

Immunomodulator activity of extracts and fractions of *Bidens pilosa L.* on human mononuclear cells and macrophages

Name of the speaker:
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Abstract
Currently, the modulation of the immune response with compounds of natural origin has been of interest in the development of new treatments for chronic diseases such as cancer and autoimmunity due to its advantages over conventional drugs (1,2).

Some molecules such as fatty acids, terpenes and flavonoids regulate the activation of antigen-presenting cells such as macrophages (3). Taking into account that their high functional plasticity promotes the pro- or anti-inflammatory response, M1 or M2, respectively in pathological contexts, are considered fundamental target cells in immunomodulation (4).

One of the medicinal plants with immunomodulatory potential is Bidens pilosa L., used in different tropical countries for its anti-inflammatory effects (5,6), however, there are few studies that evaluate its modulatory effects on macrophages, for this reason,

This study focused on evaluating the immunomodulatory effects of this plant on the polarization of human macrophages (M1-M2) obtained from humans.

As an initial screening, MTTs tests were carried out, in which it was observed that the extracts and fractions of the aerial part of the plant have low cytotoxicity on human peripheral blood mononuclear cells (PBMCs). Likewise, it was found that the petroleum ether extract, the ethyl acetate fraction and the hydroalcoholic residue have an anti-proliferative effect on these cells and modulate the production of inflammatory cytokines such as IL-6 and IL-8. Additionally, it was observed that the petroleum ether extract modulates the polarization of human macrophages towards an M2 (anti-inflammatory) profile. Likewise, the mentioned fractions also induced this profile, but to a lesser extent. The chemical characterization of the petroleum ether extract showed the presence of compounds such as: terpenes, hydrocarbons, fatty acids, in this extract, of which different anti-inflammatory properties have been reported (7-9). In the fractions, the presence of flavonoid compounds, phenolic acids and chalcones was observed, such as quercetin, caffeic acid and okanin, respectively, of which anti-inflammatory activities have also been reported (5,10-12).

Acknowledgment
I would like to thank the Pontificia Universidad Javeriana, the Ministry of Sciences, the Ministry of National Education, the Ministry of Industry, Commerce and Tourism and ICETEX, the Scientific

Ecosystem Call - Scientific Colombia “Generation of therapeutic alternatives in cancer from plants through translational research and development processes, articulated in environmentally and economically sustainable value systems” financed by the World Bank.

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Determination of the antiproliferative or proliferative activity of extracts and fractions of *Acmella ciliata* on human mononuclear cells

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Abstract
In Colombia, the use of traditional medicine is related to the biodiversity of the territory's flora, which offers an unlimited source of natural metabolites with therapeutic properties. One of the plants that has been used for different medicinal purposes in South America to treat oral pain and inflammation is Acmella ciliata (1). Some studies have shown that different components chemicals of this family can exert anti-inflammatory effects (2). The alkylamides are one of those groups bioactives that is known to regulate different mediators inflammatory, such as NF-κB, IL 1β, IL-6 and TNF-α (3,4,5).

These compounds are have identified A. ciliata, but the possible immunomodulatory effect of this and other metabolites present in Acmella on human dendritic cells (DCs), which have the function of modulating, activating and regulating immune response according to their state of maturation, has not yet been evaluated.

This activity can be interpreted in different scenarios, which is why in this work three different moments are evaluated in three different periods of concuvation, a cytotoxic activity, an evaluation against an activation of the response and an evaluation in an activated context of the immune response.

Preliminary results show that leaf and stem extracts, unlike flower essential oils, have greater immunomodulatory (proliferative) activity on PBMC at low concentrations and this may be associated with the presence of alkamides and sesquiterpenes in the extracts. Based on these results, future analyzes will focus on evaluating the possible modulating effect that more bioactive extracts could have on phenotypic maturation in DCs.

Acknowledgment:
I would like to thank the Pontificia Universidad Javeriana, the Ministry of Sciences, the Ministry of National Education, the Ministry of Industry, Commerce and Tourism and ICETEX, the Scientific Ecosystem Call - Scientific Colombia "Generation of therapeutic alternatives in cancer from plants through translational research and development processes, articulated in environmentally and economically sustainable value systems" financed by the World Bank.

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Caesalpinia spinosa plant extract P2Et exhibit tumor microenvironment intervention on a tumor cells-cancer associated fibroblasts coculture model

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Name of the speaker: Maria Camila Jimenez

Introduction

The tumor microenvironment (TME) is a complex platform where cancer associated fibroblasts and tumoral cells interacts favoring metabolic and energetic coupling. On a paracrine approach, P2Et extract have significantly attenuated the phenotypic and metabolic activation of TGF-β-treated 3T3 fibroblasts and decreased migratory and multipotent capacities of tumor cells promoted by activated fibroblasts.

Research questions

Given the backgrounds, the aim of this study was exploring the potential of P2Et and Anamú-SC extracts to inhibit/intervene the TME using a methodology representing the cell-to-cell interaction between breast cancer tumor cells and fibroblasts.

Experimental Design

Under a 3D interaction model, the metabolic and phenotypic changes were evaluated using flow cytometry and functional assays.

Results

Cell-to-cell interaction was capable to reproduce changes characteristic of CAF population with increased glucose uptake and diminished cav-1 expression on fibroblasts; also caused global IL6 transcripts increase and an incremented migration capacity on tumor cells.

P2Et and Anamú extracts reduced metabolic changes occurring during coculture, and impacted migration potential.

Conclusion

In vitro tests have demonstrated the therapeutic potential of natural products to reduce the tumor support occurring in the TME.

Effect of MSCs on angiogenesis and viability of tumor cell lines

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Abstract
Cancer is a disease in which cells grow at an uncontrolled rate and spread to other parts of the body. It affects a large part of the population and is the second leading cause of death worldwide. Different treatments have been investigated for this disease; however, the prevalence increases every day, which is why research has been carried out with natural extracts derived from plants such as *Caesalpinia Spinosa* and *Petiveria Alliacea* in breast cancer and melanoma. Within the development of cancer there are many cells that support it, such as endothelial cells, immune cells, cancer-associated fibroblasts (CAF), mesenchymal stem cells, among others. The role of mesenchymal stem cells and the release of their secretome has been widely studied due to their immunomodulatory and anti-inflammatory properties, however, their contribution to tumor progression is not clear which leads to the interest of correlate these cells with progression of the disease. The viability of tumor cells treated with mesenchymal stem cells, their secretome and the combination with the previously mentioned natural extracts was then evaluated, finding that the secretome of MSC in combination with the natural extracts decreases the viability of breast cancer and melanoma tumor cell lines. Relating to angiogenesis, the MSC´s conditioned medium decreases the capacity to form polygonal structures on MATRIGEL®, however it is possible that this is related to the decrease in the viability of the endothelial cell line in absence of serum. It remains to be demonstrated conclusively the effect of MSC´s conditioned medium supplemented with serum on viability of endothelial cells and angiogenesis potential.

This project is part of the macro-project entitled “ESTUDIO SOBRE LA REGULACION DEL MICROAMBIENTE TUMORAL POR EXTRACTOS/COMPUESTOS NATURALES DERIVADOS DE PLANTAS” which is financed by Colciencias under the framework of the Colombia Científica invitation for proposals with registration code 61884.

Modulation of the nuclear receptor PPARγ as a therapeutic target in colon cancer progression

Director: José Iglesias PhD. - Co director: Susana Fiorentino PhD.

Name of the speaker: María Paula López

Introduction

Colon cancer is a multifactorial pathology, characterized by uncontrolled proliferation of epithelial cells due to mutations in oncogenes and tumor suppressor genes. One of the molecular mechanisms involved in colon cancer progression is the peroxisome-proliferator-activated receptor gamma (PPARγ), which is the nuclear receptor that acts as a critical transcriptional regulator of lipid metabolism. Previous studies of PPARγ have shown that its activation is capable of inducing apoptosis and cell cycle arrest. However, further studies are still needed to understand its antitumor function.

In addition, extracts obtained from medicinal plants contain polyphenols and polyunsaturated fatty acids that activate PPARγ. Consequently, the effect of extracts on PPARγ activity constitutes a new therapeutic concept for the treatment of patients with colon cancer.

Research questions

What is the effect of modulation of the nuclear receptor PPARγ activity on colon cancer progression?

Experimental Design

1. Comparison of PPARγ activity from tumor and non- tumor colon samples from patients with this pathology by gene expression measurement and PPARγ reporter assays.
2. Evaluation of PPARγ activity on tumorigenic properties in colon cancer cell lines and in the murine AOM/DSS model. In addition, we will evaluate the role of PPARγ on lipid metabolism and antioxidant function in these models through biochemistry assays.
3. Evaluation of the effect of natural extracts with antitumoral background on PPARγ activity through reporter assays.

Results

We confirmed the antitumor effect of PPARγ activation in the cell lines. Furthermore, we found an increase in total fatty acid amounts and a decrease of GSH in the cell lines after PPARγ activation. Finally, we determined that the extract ¨P2Et¨ from *Caesalpinia spinosa* decreases PPARγ activity.

Conclusions

These results suggest that the antitumor activity of PPARγ in colon cancer occurs through a pro-oxidant effect that could involve lipid metabolism. Furthermore, the antitumor effect of P2Et extract is PPARγ independent.

Evaluation of in vitro culture systems for the detection of neoantigen-specific T cells from healthy donors.

Aurthors: Laura Camila Martinez Enriquez[1] y Carlos Parra-López[2]

Name of the speaker:
Laura Camila Martinez Enriquez

Abstract

Immunotherapy based on neoantigens stimulates the immune system of cancer patients by inducing a directed antitumor response mediated by T lymphocytes. Neoantigens are generated by somatic mutations in DNA that produce changes in the amino acid sequence and are exclusive to tumor cells. The evaluation of the immunogenicity of these neoantigens is generally performed *in vitro* using patient's cells, however, the frequency of responses to neoantigens in these assays is low. The use of T cells from healthy donors represents an alternative the screening and evaluation of immunogenicity of neoantigens. This study proposes the evaluation of different culture systems to detect T cells from healthy donors specific for neoantigens. We used peripheral blood mononuclear cells (PBMCs) from healthy HLA-A*02:01 donors. Three different types of cultures were evaluated, maintaining the use of the cytokines IL-21, IL-15 and IL-7 but modifying the starting cells: i) total PBMCs, ii) accelerated co-culture with dendritic cells (acDCs) from PBMCs and iii) co-culture of dendritic cells (DCs) with naïve CD8 T cells. HLA-A*02:01-restricted neoantigens were selected from a literature review and evaluated as a pool. Recognition of CD8+ T cells to neoantigens was assessed by IFN-y production and by tetramer labeling. As results, it was possible to observe that the presence of professional presenting cells, such as DCs, and an enrichment of naïve CD8 T cells is necessary, since it was only possible to detected in this system, although in low proportion, specific neoantigen T cells. These results were only observed in 2 out of 4 donors evaluated, which indicates that additional experiments and replicates are necessary to determine if this system is suitable. This study demonstrates the high complexity of using cells from healthy donors, however, it is a promising source of immune cells since it would not only allow the evaluation of the immunogenicity of neoantigens but also the identification of specific TCRs against these peptides for of TCR modification-based cell adoptive therapy.

References

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Analysis of the effect of the of the extract P2Et on, myeloid-derived suppressor cells (MDSC) in a murine melanoma model

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Speaker: Jhon Jairo Calderón Pérez

Introduction

Within the tumor microenvironment, myeloid-derived suppressor cell (MDSC)-mediated immunosuppression has a critical role in tumor progression. It has been described that tumor cells augment oxidative stress and increase the suppressive function of MDSCs through transmissible ER stress (TERS) in the tumor microenvironment. In this sense, by eliminating TERS or using antioxidants, MDSCs decrease their immunosuppressive phenotype and become cells capable of activating the immune response against the tumor, so targeting this TERS may be important for the reprogramming of these cells. In the Immunobiology and Cell Biology group we have worked with the P2Et extract of the plant *Caesalpinia spinosa*, which has been observed to modulate reticulum stress and present antioxidant properties *in vitro* in B16 cells and decrease MDSC infiltration in melanoma model *in vivo*.

Aim

Determine the impact of P2Et extract treatment on TERS towards MDSC and its suppressive activity in a murine melanoma model?

Experimental Design

BM-MDSCs generated by differentiation of C57BL/6 bone marrow cells using IL-6 and GM-CSF during 4 days were used, then treated for 24h with conditioned medium of murine melanoma tumor cells (B16) pretreated with P2Et or their respective controls. The phenotype was verified by flow cytometry. To observe ER stress induction, qPCR and western blotting targeting proteins and genes involved in the UPR pathway were performed. For functional assays, a suppression assay was performed on T Cells extracted from fresh spleens of C57BL/6 mice at different MDSC: T cells ratios (1:4, 1:16, 1:32).

Results

Direct treatment with P2Et was found to have the ability to induce a PMN-MDSC phenotype. Additionally, P2Et conditioned medium were observed to exhibit lower TERS towards MDSCs accompanied with a reduction in PD-L1, iNOS, Arg1 and a lower suppressive effect on CD4+ and CD8+ T Cells, showing the potential of P2Et on modulating MDSC plasticity.

Conclusion

The effect of direct P2Et as well as its conditioned medium on MDSCs can be observed, obtaining less stressed cells and with a lower suppressive capacity on CD4+ and CD8+ LT, indicating a potential therapeutic use to target these cells.

Standardization of the murine model of AML for the evaluation of the antileukemic activity of plant extracts

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Name of the speaker: Natalia Alejandra Murillo Vallejo, cpHD

Acute myeloid leukemia (AML) is a tumor of hematopoietic origin that is generated in the bone marrow by neoplastic transformation of myeloid stem cells, due to mutations that cause a blockage in differentiation, thus an alteration in maturation, and a proliferative imbalance. To date, first-line treatment of AML is based on the use of chemotherapeutics: daunorubicin and cytarabine. However, the rate of complete remission is not optimistic. Among the hallmarks of leukemic cell cancer that have been associated with poor response to conventional treatment and disease progression are metabolic reprogramming and evasion of the immune response.

To test this hypothesis, we standardized a murine model of AML developed by intravenous inoculation of DA3ER cells in BALB/c mice to evaluate the anti-leukemic activity of different plant extracts that can modulate metabolism and activate the anti-tumor immune response.

The extracts evaluated were Anamu-SC and P2Et which showed that, at the end of the model, the extracts managed to maintain hematological values such as hemoglobin, hematocrit and red blood cell count (RBC) towards the normal range in comparison with the control animals (PBS 1X).

Additionally, regarding the number of blasts in peripheral blood we found a decrease on days 17 and 20 in Anamu treated animals. However, in the rest of the evaluations no clear differences were observed.

Finally, in the evaluation of metastasis to different organs we found a significant decrease in the number of tumor cells in the animals treated with Anamu and P2Et, compared to PBS.

Antitumor effects of the ethanolic extract from *Tillandsia usneoides* and *Piper nigrum* in the breast cancer and melanoma murine models

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Name of the speaker: Paola Lasso

Introduction
The main limits of current antitumor therapies are tumor heterogeneity, chemoresistance, relapses and toxic effects that impair a patient's quality of life. Therefore, the discovery of therapeutic alternatives, such as adjuvants to conventional therapy that modulate the intracellular oxidation state, or the immune response activation remains a challenge. Thanks to the traditional medicine, several uses of plants such as *P. nigrum* and *T. usneoides* are known, indicating a promising antitumor effect.

Research questions
To evaluate the antitumor and immunomodulatory activity of ethanolic extracts of *T. usneoides* and *P. nigrum* in murine models of breast cancer and melanoma.

Experimental Design
For breast and melanoma tumor induction, 4T1 and B16-F10 cells were inoculated in BALB/c and C57BL/6 mice, respectively. Mice were treated two times per week with PBS (negative control), P2Et (positive control), *T. usneoides* or *P. nigrum* and the size of the tumors was assessed three times per week. Mice were euthanized by CO_2 inhalation, and the spleen and tumor were removed and processed. Cells were stained according to the designed multicolor panels and acquired by flow cytometry.

Results
In the *in vivo* model of breast cancer, a significant decrease in tumor size was found in the animals treated with the two extracts compared to the PBS group. However, in the murine melanoma model, only the *P. nigrum* extract had a significant antitumor effect. Tumor microenvironment evaluation showed an increase in dendritic cells and activated $CD8^+$ T cells, and a decrease in myeloid-derived suppressor cells (MDSC) and Tregs in the animals treated with *P. nigrum* (in both models) and *T. usneoides* (breast cancer model).

Conclusion

The extracts of *T. usneoides* and *P. nigrum* presented a promising antitumor effect, possibly due to the induction of an effector immune response and the modulation of the suppressive immune response.

Automatic metabolite quantification in proton NMR spectra of urine samples

Autors: Bolaños, J Alejandro; Wist, Julien - Universidad del Valle - Faculty of Natural and Exact Sciences - Department of Chemistry

Name of the speaker:
Bolanos, J Alejandro

Abstract
Metabonomics is a complementary science to the other `-omics' sciences with a broad spectrum of applications ranging from basic biology to applied sciences such as medicine and toxicology. After mass spectrometry, nuclear magnetic resonance spectroscopy is one of the main platforms for metabonomic analysis. Various tools have been developed in the framework of the identification of metabolites in mixtures, compiling reference libraries from existing repositories, however, recent comparisons show that identification continues to be the bottleneck in metabonomic studies. This project aims to design an automatic quantification methodology as a tool to reduce the level of expertise in the processing of biological fluid NMR spectra and increase the reliability of the data generated. By automatic peak detection and candidate selection, several metabolites had been included in the quantification list and the results are compared with the manual assignment. Currently, a database of curated metabolite assignments is generated in order to train a chemical shift predictor to improve the candidate selection step.

Physicochemical, dendritogenic and toxicological evaluation of an extract rich in flavonoids from *Passiflora edulis f edulis sims.*

Rodriguez Alex[1], Albarracín Sonia Luz[1].

[1]: Grupo de investigación en bioquímica experimental y computacional, laboratorio de neurobioquimica, Pontificia Universidad Javeriana.

Name of the speaker:
Alex Rodríguez Usaquén

Abstract
The *Passiflora* genus is made up of different species widely related with traditional knowledge and importance of their economic use, whose fruits and leaves have exhibited significant activity as an antioxidant, sedative, tranquilizer among others. Since some compounds with activity in the central nervous system have been identified, in this work the physicochemical and biological characteristics and the toxicity of an aqueous extract of *Passiflora edulis f edulis sims* leaves were evaluated. Evaluated in primary culture neurons from Wistar rat embryos of 18 days (E18). It was established that the extract retains an activity on the induction of the complexity of the dendritic tree with different batches produced at different times and that the addition of a flavonoid with dendritogenic activity, previously reported, rutin, did not exert a synergistic effect.

For the chemical analysis, chromatographic studies were used by HPTLC, UPLC-DAD, and UPLC-MS, which allowed establishing the typical profile of the extract and it was found to be consistent in the different batches evaluated, as well as in the butanolic fraction.

Finally, following the guidelines of the OECD (Organization for Cooperation for Economic Development), the acute toxicity study was carried out with the aqueous extract of *Passiflora edulis f. edulis sims.*

Globally, the physicochemical results show that the production of the *Passiflora edulis f edulis sims* extract under standardized conditions guarantees the conservation of the composition of secondary metabolites, which, when biologically evaluated "in vitro", induce dendritogenic activity, while those profiled in acute toxicity show a higher LD50 at 2000 mg/kg, and in toxicity at repeated doses of 1000 mg/kg for 28 days, it manifests with a mild focal periportal lymphocytic infiltrate and incipient increases in the focal corticomedullary nephrocalcinosis typical of the species.

Determination of the composition of flavonoids in leaves of *G. angustifolia* Kunth in natural guaduales of the department of Nariño

Hair Santiago Lozano Puentes[1], Geison Modesti Costa[2], Lucia Ana Díaz Ariza[3]
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Name of the speaker:
Hair Santiago Lozano Puentes

Flavonoids are a group of polyphenolic compounds produced in plants as secondary metabolites. Various biological activities already described for these metabolites are antimicrobial, anti-inflammatory, cardioprotective, antidiabetic, and anticancer properties. *Guadua angustifolia* Kunth is a bamboo endemic to America and is considered native to Colombia, for which there are few scientific studies about its chemical composition and biological activities, mainly in natural guaduales in the department of Nariño. Therefore, this work aimed to analyze the composition of flavonoids in *G. angustifolia* Kunth leaves in natural guaduales in the department of Nariño, Colombia. For this purpose, leaves were collected from 3 adult culms of 26 natural guaduales of *G. angustifolia* Kunth in 9 municipalities of the department of Nariño. Ultrasound-assisted extraction of flavonoids was performed using chloroform, methanol, and water 2:1:1 as solvents. Subsequently, the complexation method with $AlCl_3$ was used to estimate the concentration of flavonoids and Ultra Efficiency Liquid Chromatography coupled to a photodiode array detector (UPLC-PDA) for the identification of these metabolites. A flavonoid concentration range between 0.14 to 4.11 mg EQr/g plant material was found. These values are higher than those reported by Mosquera and collaborators in 2015, in the culms of *G. angustifolia* Kunth collected in the department of Quindío. The municipalities that presented the highest concentration of flavonoids were San Lorenzo and La Florida. By UPLC, it was possible to identify the absorption spectrum confirming the presence of different flavonoids in the samples evaluated. It is important to highlight that depending on the collection municipality, the composition of flavonoids changes. These changes can be attributed to the characteristics of the phytobiome, that is, the interaction between plants, their environment, and the complex communities of organisms that influence plant health and productivity. More studies are required to determine which parameters influence the composition of flavonoids, focusing on the large-scale production of these metabolites.

The GAT Bioinformatics Platform

Rafael A. González and Néstor A. Nova - Pontificia Universidad Javeriana

Name of the speaker:
Rafael A. González Rivera

Introduction

Conducting effective cancer research requires open, multidisciplinary, multi-institutional collaboration with a wide variety and volume of data. In the context of the GAT research ecosystem, a bioinformatics platform was developed including tools and portals for supporting experiments, reports, publications and collaboration. The platform has been developed and evaluated iteratively, both in terms of acceptance as well as its contribution to the cohesiveness of the research network.

Research questions

How does a collaborative bioinformatics platform contribute to the effective research and development of a translational cancer research ecosystem?

Experimental design

The platform was developed in an iterative way through several phases: (1) initial high-level design and benchmarking with respect to other platforms; (2) participative requirements analysis and design together with researchers; (3) progressive setup of each project, including data; (4) technology acceptance evaluation; (5) social network analysis of the collaboration dynamics in the research ecosystem.

Results

Results show that the platform becomes integrated and essential to the research and management of the ecosystem. Several projects and researchers have uploaded their data and use the platform for recording, visualizing and sharing experimental results, as well as sharing and creating academic and administrative documents. Adoption has been uneven and different projects and researchers will adopt at different times and with different purposes.

Conclusion

A digital space for collaboration has not only been useful but essential, something acutely seen during the COVID-19 pandemic. The platform operates at the same time with parallel tools, some of which are not even known in advance. Its ultimate success is dynamic and should be continually evaluated.