Informe de Actividades 2022 y Planificación futura de la Cátedra UAM-Fundación Instituto Roche de Medicina Personalizada de Precisión

Diciembre de 2022

Apartados

Generación de Conocimiento

1. Publicación del artículo científico " Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A "

Nature Communications (IF: 14.92; **Q1**)

nature communications

Article

https://doi.org/10.1038/s41467-022-35065-z

Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A

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Precision oncology research is challenging outside the contexts of oncogenic addiction and/or targeted therapies. We previously showed that phosphoproteomics is a powerful approach to reveal patient subsets of interest characterized by the activity of a few kinases where the underlying genomics is complex. Here, we conduct a phosphoproteomic screening of samples from HER2-negative female breast cancer receiving neoadjuvant paclitaxel ($N = 130$), aiming to find candidate biomarkers of paclitaxel sensitivity. Filtering 11 candidate biomarkers through 2 independent patient sets ($N = 218$) allowed the identification of a subgroup of patients characterized by high levels of CDK4 and filamin-A who had a 90% chance of achieving a pCR in response to paclitaxel. Mechanistically, CDK4 regulates filamin-A transcription, which in turn forms a complex with tubulin and CLIP-170, which elicits increased binding of paclitaxel to microtubules, microtubule acetylation and stabilization, and mitotic catastrophe. Thus, phosphoproteomics allows the identification of explainable factors for predicting response to paclitaxel.

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Dos de las figuras clave son las siguientes:

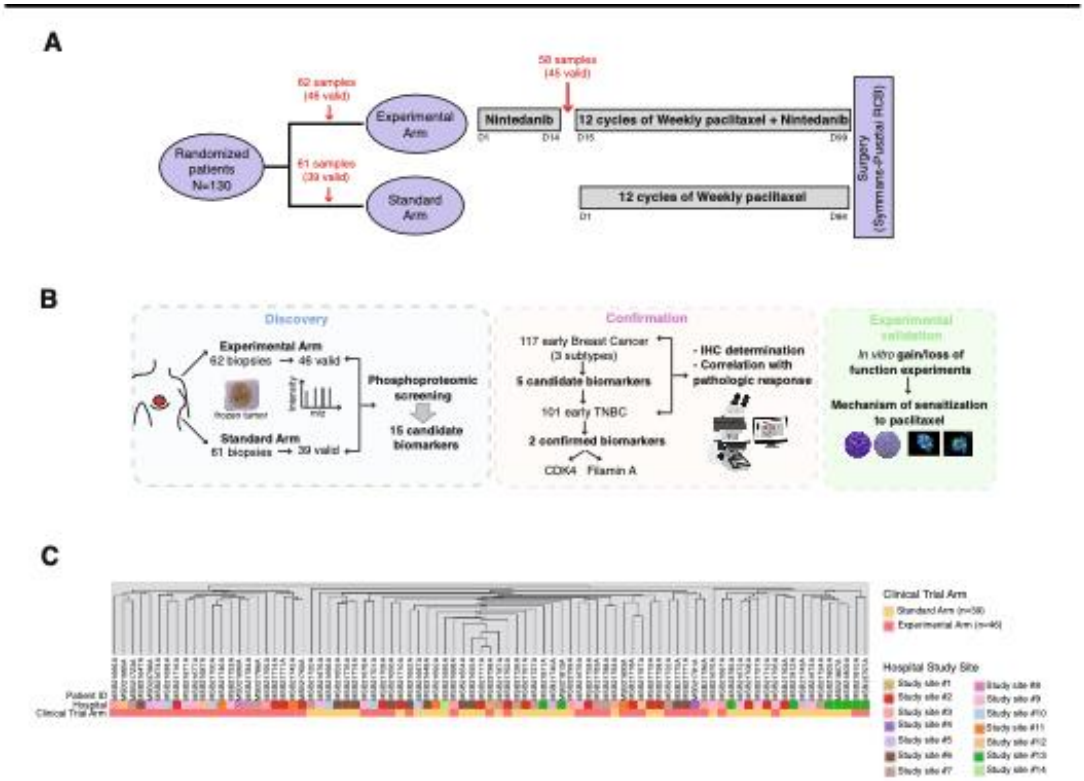

Fig. 1 | Clinical trial tumour samples: the phosphoprofiles were independent of the study site and/or treatment arm. A Clinical trial treatment and sampling schedule. After randomization, patients were scheduled for a fresh tumour biopsy. Sixty-two and sixty-one patients allocated to the Experimental and Standard arms, respectively, consented to and underwent a baseline biopsy (out of 130 patients). Patients allocated to the experimental arm underwent a 2-week course of single-agent nintedanib (150 mg orally twice a day), and then a second tumour sample was harvested (N = 58 patients consented to this second biopsy) prior to undergoing 12 weekly courses of paclitaxel combined with nintedanib. Those allocated to the standard arm immediately started weekly paclitaxel without the 14-day delay and did not have a second tumour sample harvested. The endpoint (tumour response according to the RCB score) was determined at the time of surgery, and patients then received standard treatment according to the referring physician's choice (radiation or hormonal therapy or further chemotherapy if indicated). **B** Flow chart depicting the study steps: biomarker discovery, biomarker confirmation and experimental validation. **C** Unsupervised hierarchical clustering. A phosphopeptide intensity data matrix was used for clustering analysis. Patient IDs are listed horizontally. The two following rows indicate, for each sample, whether they were allocated to the standard or experimental arm and the study site origin.

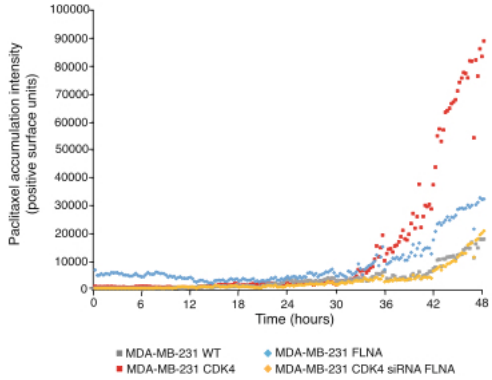

Fig. 6 | Tubulin and filamin A form a complex with CLIP170, which elicits increased binding of paclitaxel to microtubules F Paclitaxel-binding experiment. Fluorescently labelled paclitaxel was added to live cultures of MDA-MB-231 WT, CDK4 or FLNA cells. MDA-MB-231 CDK4 cells with filamin A knockdown were added to the experiment as well. The greater the green signal is, the higher the amount of paclitaxel bound to microtubules. It can be appreciated how both CDK4- and fila- min A-overexpressing cell lines display both earlier and higher paclitaxel binding. Scale bar: 75 μm. The chart on the right-hand side depicts the signal (in fluorescent surface units) tracing paclitaxel accumulation over the 48-h time course, displaying a clear increase in the two overexpressing transfectants (CDK4 and FLNA) com- pared to the parental cell line and a reversion of the phenotype by filamin A knockdown in MDA-MB-231 CDK4 cells.

2. Publicación del artículo científico "Peripheral Blood Mononuclear Cells Predict Therapeutic Efficacy of Immunotherapy in NSCLC"

Cancers (Basel) (IF: 6.13; **Q1**)

cancers

MDPI

Article

Peripheral Blood Mononuclear Cells Predict Therapeutic Efficacy of Immunotherapy in NSCLC

Jacobo Rogado [1,2,*], Fernando Pozo [3], Kevin Troule [3], José Miguel Sánchez-Torres [2,4], Nuria Romero-Laorden [2,4], Rebeca Mondejar [2,4,5], Olga Donnay [2,4], Anabel Ballesteros [2,4], Vilma Pacheco-Barcia [2,6], Javier Aspa [2,7], Fátima Al-Shahrour [3], Arantzazu Alfranca [2,8] and Ramon Colomer [2,4,5]

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Citation: Rogado, J.; Pozo, F.; Troule, K.; Sánchez-Torres, J.M.; Romero-Laorden, N.; Mondejar, R.; Donnay, O.; Ballesteros, A.; Pacheco-Barcia, V.; Aspa, J.; et al. Peripheral Blood Mononuclear Cells Predict Therapeutic Efficacy of Immunotherapy in NSCLC. *Cancers* **2022**, *14*, 2898. https://doi.org/10.3390/cancers14122898

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Simple Summary: Biomarkers to guide clinical decisions and efficacy are limited in advanced non-small cell lung cancer's anti-PD-1 immune checkpoint inhibitors. We prospectively explored baseline peripheral blood mononuclear cells in order to asses' immunotherapy predictors in this setting. We included 39 patients diagnosed with non-small cell lung cancer treated with immunotherapy in the study group and 40 patients with advanced malignancies treated with non-immunotherapy treatment, as control group. We detected that high baseline levels of circulating T cell subpopulations related to tissue lymphocyte recruitment are associated with poorer outcomes of immunotherapy-treated advanced non-small cell lung cancer patients, and these differences were specific to immunotherapy-treated patients.

Abstract: In lung cancer immunotherapy, biomarkers to guide clinical decisions are limited. We now explore whether the detailed immunophenotyping of circulating peripheral blood mononuclear cells (PBMCs) can predict the efficacy of anti-PD-1 immunotherapy in patients with advanced non-small-cell lung cancer (NSCLC). We determined 107 PBMCs subpopulations in a prospective cohort of NSCLC patients before starting single-agent anti-PD-1 immunotherapy (study group), analyzed by flow cytometry. As a control group, we studied patients with advanced malignancies before initiating non-immunotherapy treatment. The frequency of PBMCs was correlated with treatment outcome. Patients were categorized as having either high or low expression for each biomarker, defined as those above the 55th or below the 45th percentile of the overall marker expression within the cohort. In the study group, three subpopulations were associated with significant differences in outcome: high pretreatment levels of circulating CD4+CCR9+, CD4+CCR10+, or CD8+CXCR4+ T cells correlated with poorer overall survival (15.7 vs. 35.9 months, HR 0.16, $p = 0.003$; 22.0 vs. NR months, HR 0.10, $p = 0.003$, and 22.0 vs. NR months, HR 0.29, $p = 0.02$). These differences were specific to immunotherapy-treated patients. High baseline levels of circulating T cell subpopulations related to tissue lymphocyte recruitment are associated with poorer outcomes of immunotherapy-treated advanced NSCLC patients.

La figura más relevante del artículo es la siguiente:

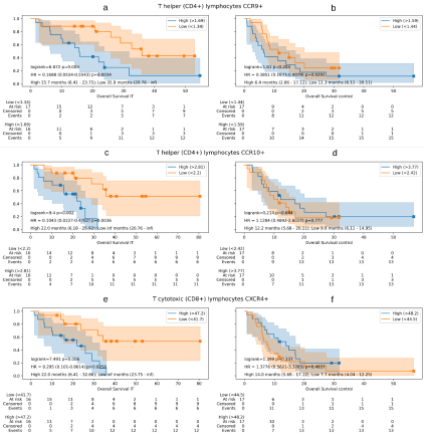

Figure 1. Overall survival Kaplan–Meier curves showing overall survival differences between immunotherapy treatment (IT) study group versus control group. The Kaplan–Meier curves show the differences in survival according the high or low expression of each peripheral blood mononuclear cell subpopulation studied in both groups. In addition, the log-rank test, multivariate cox regression models, and the median overall survival values with their range are reflected. Graphics (**a**,**b**) show overall survival in immunotherapy treatment group (**a**) versus study group (**b**) according to the expression of T-helper lymphocytes CCR9+. Graphics (**c**,**d**) show overall survival in immunotherapy treatment group (**c**) versus study group (**d**) according to the expression of T-helper lymphocytes CCR10+. Graphics (**e**,**f**) show overall survival in immunotherapy treatment group (**e**) versus study group (**f**) according to the expression of T-cytotoxic lymphocytes CXCR4+.

3. Publicación del artículo de revisión "The Homologous Recombination Deficiency Scar in Advanced Cancer: Agnostic Targeting of Damaged DNA Repair"

Cancers (Basel) (IF: 6.13; **Q1**

cancers

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Review

The Homologous Recombination Deficiency Scar in Advanced Cancer: Agnostic Targeting of Damaged DNA Repair

Vilma Pacheco-Barcia [1], Andrés Muñoz [2], Elena Castro [3], Ana Isabel Ballesteros [4], Gloria Marquina [5], Iván González-Díaz [6], Ramón Colomer [4] and Nuria Romero-Laorden [4,*]

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Citation: Pacheco-Barcia, V.; Muñoz, A.; Castro, E.; Ballesteros, A.I.; Marquina, G.; González-Díaz, I.; Colomer, R.; Romero-Laorden, N. The Homologous Recombination Deficiency Scar in Advanced Cancer: Agnostic Targeting of Damaged DNA Repair. *Cancers* **2022**, *14*, 2950. https://doi.org/10.3390/cancers14122950

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Simple Summary: Tumor-suppressor genes are involved in DNA break repair through the homologous recombination system and are widely known for their role in hereditary cancer. Beyond breast and ovarian cancer, prostate and pancreatic cancer also have targetable homologous recombination deficiency (HRD) beyond the well-known *BRCA1* and *BRCA2* with relevance that exceeds diagnostic purposes. In this review, we aim to summarize the roles of HRD across tumor types and the treatment landscape to guide the targeting of damaged DNA repair based on the cancer's genetic features.

Abstract: *BRCA1* and *BRCA2* are the most recognized tumor-suppressor genes involved in double-strand DNA break repair through the homologous recombination (HR) system. Widely known for its role in hereditary cancer, HR deficiency (HRD) has turned out to be critical beyond breast and ovarian cancer: for prostate and pancreatic cancer also. The relevance for the identification of these patients exceeds diagnostic purposes, since results published from clinical trials with poly-ADP ribose polymerase (PARP) inhibitors (PARPi) have shown how this type of targeted therapy can modify the long-term evolution of patients with HRD. Somatic aberrations in other HRD pathway genes, but also indirect genomic instability as a sign of this DNA repair impairment (known as HRD scar), have been reported to be relevant events that lead to more frequently than expected HR loss of function in several tumor types, and should therefore be included in the current diagnostic and therapeutic algorithm. However, the optimal strategy to identify HRD and potential PARPi responders in cancer remains undefined. In this review, we summarize the role and prevalence of HRD across tumor types and the current treatment landscape to guide the agnostic targeting of damaged DNA repair. We also discuss the challenge of testing patients and provide a special insight for new strategies to select patients who benefit from PARPi due to HRD scarring.

Una de las figuras clave es la siguiente:

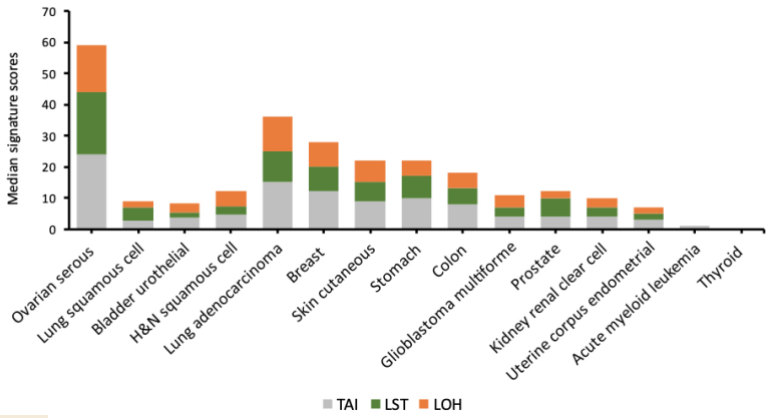

Figure 3

HRD prevalence across different tumor types. Adapted from Marquard et al. [21], copyright 2015 Marquard et al, under the Creative Commons Attribution Non-commercial No Derivatives 4.0 License (https://creativecommons.org/licenses/by-nc-nd/4.0/, accessed on 12 May 2022). The figure has been made for the purposes of this review. HRD analysis of TCGA samples across 15 different cancer types was performed based on the number of Telomeric Allelic Imbalances (TAI) based on a genomic scar accumulation, the large scale transition (LST) based on a type of genomic scar associated with loss of BRCA1 or BRCA2 and the HRD-LOH based on a scar enriched in high-grade serous ovarian cancer patients with a loss of BRCA1 or BRCA2 [21,22,23]. However, the method originally used for ovarian cancer samples was adapted to avoid bias when the algorithm is applied across different tumors: (1) In the original publication describing TAI [24], all allelic imbalance events that extended to the telomere were counted, if they did not span the centromere. This results in an overrepresentation of tumors with an uneven copy number among high TAI cases, which has been corrected in the method used for the present study. (2) The original publication describing HRD-LOH [23] excluded chromosome 17 because LOH on chromosome 17 in the ovarian cancer samples is ubiquitous and for this reason did not provide independent information. However, for this figure, chromosome 17 was not excluded, as chromosome 17 is not ubiquitously lost in all cancer types, and therefore may provide independent information in some tumor samples.

4. Publicación del artículo científico "Tumor P70S6K hyperactivation is inversely associated with tumor-infiltrating lymphocytes in triple-negative breast cancer"

Clinical and Translational Oncology (IF: 3.4; **Q3**)

Clinical and Translational Oncology
https://doi.org/10.1007/s12094-022-03006-3

BRIEF RESEARCH ARTICLE

Tumor P70S6K hyperactivation is inversely associated with tumor-infiltrating lymphocytes in triple-negative breast cancer

Rebeca Jimeno[1] · Silvana Mouron[1] · Roberto Salgado[2,3] · Sherene Loi[2,4] · Belén Pérez-Mies[5,6,7] · Rodrigo Sánchez-Bayona[8] · Luis Manso[8] · Mario Martínez[9] · Ana Garrido-García[10] · Rosario Serrano-Pardo[11] · Ramón Colomer[10,12] · Miguel Quintela-Fandino[1,13,14]

Received: 24 August 2022 / Accepted: 7 November 2022

Abstract

Purpose Triple-negative breast cancer (TNBC) is characterized by large heterogeneity and relative lack of available targeted therapies. To find therapeutic strategies for distinct patients with TNBC, several approaches have been used for TNBC clustering, including recently immune and phosphoproteomic patterns. Based on 70-kDa ribosomal protein S6 kinase (P70S6K)-TNBC clustering, the current study explores the immune profiling in TNBC tumors.

Methods Stromal tumor-infiltrating lymphocytes (sTILs) were evaluated in human TNBC tumor samples. Furthermore, immunohistochemistry staining for CD8, CD4, Foxp3, and CD20 was performed in tissue microarrays (TMA) sections.

Results Histological analysis showed decreased sTILs, $CD20^+$ cells, and $CD8^+/CD4^+$ ratio in high phosphorylated P70S6K (p-P70S6K) tumors. Moreover, p-P70S6K score was directly correlated with $CD4^+$ and $Foxp3^+$ T cells, while it was inversely correlated with $CD8^+/CD4^+$ and $CD8^+/Foxp3^+$ ratios.

Conclusion sTIL infiltration and lymphocyte profiling vary in the context of hyperactivation of P70S6K in TNBC tumors.

Keywords TNBC · P70S6K · TIL · T cells · B cells

Introduction

Triple-negative breast cancer (TNBC) is an aggressive breast cancer (BC) subtype frequently associated to rapid progression and high rate of early recurrences and metastasis in brain, liver, and lung [1–5]. Due to its poor differentiation and molecular heterogeneity, TNBC is challenging to treat and responses to treatment are frequently short-lasting.

Several approaches based on gene expression patterns, transcriptomic profiling and other strategies have been implemented for TNBC clustering. Lately, immunogenic profile has been used to classify TNBC tumors, which have

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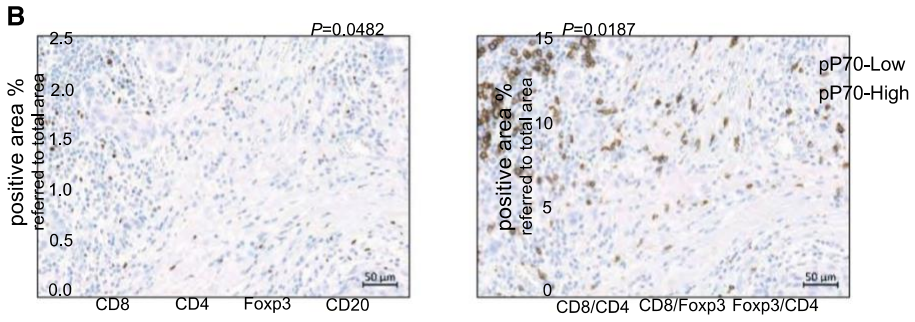
Published online: 12 December 2022

Una de las figuras clave es la siguiente



5. Publicación del artículo científico "Excess weight and anti-PD-1 immune checkpoint inhibitor's outcomes in non-small cell lung cancer"

Clinical and Translational Oncology (IF: 3.4; **Q3**)

Clinical and Translational Oncology (2022) 24:2241–2249
https://doi.org/10.1007/s12094-022-02887-8

RESEARCH ARTICLE

Excess weight and anti-PD-1 immune checkpoint inhibitor's outcomes in non-small cell lung cancer

Jacobo Rogado[1,2] · Fernando Pozo[3] · Kevin Troulé[3] · José Miguel Sánchez-Torres[2,4] · Nuria Romero-Laorden[2,4] · Rebeca Mondejar[2,4,5] · Olga Donnay[2,4] · Anabel Ballesteros[2,4] · Vilma Pacheco-Barcia[2,6] · Javier Aspa[2,7] · Fátima Al-Shahrour[3] · Arantzazu Alfranca[2,8] · Ramon Colomer[2,4,5]

Received: 19 May 2022 / Accepted: 5 July 2022 / Published online: 23 July 2022

Abstract

Purpose Immune checkpoint inhibitors are one of the most effective treatments available in advanced non-small cell lung cancer. However, at present, there are no clinical or analytical biomarkers that define which patients benefit with certainty from these treatments. In our study, we evaluated whether excess weight could be a good predictive biomarker of benefit from these drugs.

Methods We studied a population of 79 patients, divided into a study group with 39 patients diagnosed with non-small cell lung cancer treated with immunotherapy and 40 patients in a control group, diagnosed with different advanced cancers, treated with non-immunotherapy treatment. We analyzed according to the presence of excess weight or not, the treatment's outcome in the study group and in the control group (objective response, and progression-free and overall survival).

Results In our study, we detected a better response rate to immunotherapy in patients with excess weight (62.50 vs 26.08%, OR 4.72, $p=0.02$), and a better median progression-free survival (14.19 vs 5.03 months, HR 0.50, $p=0.058$) and median overall survival (33.84 months vs 20.76 months, HR 0.43, $p=0.01$) in the study group. These findings were specific to the immunotherapy group since in the control group, with patients who did not receive immune checkpoint inhibitors, these findings were not found.

Conclusion Our study suggests that patients with excess weight who receive anti-PD-1 immune checkpoint inhibitors diagnosed with non-small cell lung cancer have a better outcome. This effect is specific to patients receiving immunotherapy.

Keywords Non-small cell lung cancer · Excess weight · Immunotherapy · Immune checkpoint inhibitors · Outcome predictors

Introduction

Usually, obesity (body mass index -BMI- ≥ 30 kg/m2) has always been associated as a worse prognosis factor in many diseases. Currently, this spectrum is being broadened in recent years to excess weight, (BMI ≥ 25 kg/m2) [1–3]. In the case of cancer, specifically, it has been associated with a worse prognosis, probably, on the one hand, due to greater toxicity detected with any systemic treatment received, since a drug tissue's accumulation could be developed [4, 5], or

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La figura clave es esta:

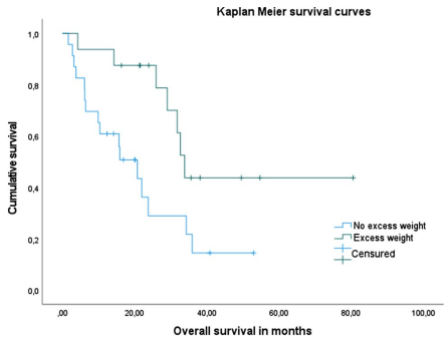

Fig. 2 Overall survival according to the presence or not of excess weight in the study group treated with immunotherapy

6. Publicación del artículo científico " Expert consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology on the determination of biomarkers in pancreatic and biliary tract cancer "

Clinical and Translational Oncology (IF: 3.4; **Q3**)

Clinical and Translational Oncology (2022) 24:2107–2119
https://doi.org/10.1007/s12094-022-02873-0

SPECIAL ARTICLE

Expert consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology on the determination of biomarkers in pancreatic and biliary tract cancer

Ruth Vera[1] · Carolina Ibarrola-de-Andrés[2] · Jorge Adeva[3] · Judith Pérez-Rojas[4] · Pilar García-Alfonso[5] · Yolanda Rodríguez-Gil[2] · Teresa Macarulla[6] · Teresa Serrano-Piñol[7] · Rebeca Mondéjar[8] · Beatriz Madrigal-Rubiales[9]

Received: 9 May 2022 / Accepted: 6 June 2022 / Published online: 25 August 2022

Abstract
Pancreatic cancer and biliary tract cancer have a poor prognosis. In recent years, the development of new diagnostic techniques has enabled the identification of the main genetic alterations involved in the development of these tumours. Multiple studies have assessed the ability of certain biomarkers, such as *BRCA* in pancreatic cancer, *IDH1* or *FGFR2* in biliary tract cancer and microsatellite instability or *NTRK* fusions in an agnostic tumour fashion, to predict response to treatment.
In this consensus, a group of experts selected by the Spanish Society of Medical Oncology (SEOM) and the Spanish Society of Pathology (SEAP) reviewed the role played by these mutations in the process of carcinogenesis and their clinical implications. As a result, this article proposes a series of recommendations to optimize the determination of these biomarkers to help standardize the diagnosis and treatment of these tumours.

Keywords Molecular diagnosis · Targeted therapies · Prognostic value · Predictive value · Pancreatic cancer · Biliary tract cancer

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9 Río Hortega University Hospital, Spanish Society of Pathology (SEAP), Valladolid, Spain

Introduction

Pancreatic and biliary tract cancers (BTCs) have a poor prognosis and are leading causes of cancer-related death [1]. Pancreatic cancer was responsible for 6.7% of cancer deaths in Spain in 2020, and BTC accounted for 4.9% [2].

Advances in diagnostic techniques and molecular biology in recent years have enabled a better understanding of the main molecular alterations involved in the development of these tumours. This consensus reviews the main recommendations regarding the determination of these molecular alterations in pancreatic and BTCs, the frequency of these alterations and the role these alterations play in the process of carcinogenesis, as well as their clinical implications.

Multiple studies have explored predictive biomarkers of responses to specific therapies (chemotherapy, immunotherapy or targeted therapy). The most prominent of these biomarkers in pancreatic cancer are breast cancer gene (*BRCA*) 1 and 2 mutations, which are associated with greater therapeutic benefit under treatment with platinum-based chemotherapy and poly-ADP-ribose polymerase (PARP) inhibitors [3, 4]. For BTC, mutations in isocitrate dehydrogenase-1 (*IDH1*) have been associated with greater clinical benefits

Destaca la table siguiente

Table 4 Current clinical application of next-generation sequencing in the treatment of intrahepatic, extrahepatic and gallbladder carcinoma of the bile duct

Gen	Alteration	Prevalence		Method	Level of evidence ESCAT[1]/ASCO[2]	Drugs
		EH and gallbladder	IH			
IDH1	Mutation	3%	10–20%	NGS	IA[1] Strong recommendation[2] High quality of evidence[2]	Ivosidenib
FGFR2	Fusion/rearrangement	1%	4–15%	NGS	IB[1]	Pemigatinib, infigratinib
NTRK	Fusion/rearrangement	2%	2%	NGS/IHC	IC[1] Moderate recommendation[2] Low quality of evidence[2]	Larotrectinib and entrectinib
MLH1, MSH2, MSH6, PMS2, EPCAM	Mutation (MSI-H)	0.5-2%	1%	NGS/IHC	IA[1] Strong recommendation[2]	Pembrolizumab (aPD1)

aPD1 anti-programmed cell death protein 1, *EH* extrahepatic, *EPCAM*: epithelial cellular adhesion molecule, *FGFR2* fibroblast growth factor receptor-2, *ICI* immune checkpoint inhibitor, *IDH1* isocitrate dehydrogenase-1, *IH* intrahepatic, *IHC* immunohistochemistry, *MLH1* MutL homolog 1, *MSH2* MutS homolog 2, *MSH6* MutS homolog 6, *MSI-H* microsatellite instability-high, *NGS* next-generation sequencing, *NTRK* neurotrophic tyrosine receptor kinase, *PMS2 PMS1* homolog 2, mismatch repair system component

[1]ESCAT scale for clinical actionability of molecular targets of the European Society for Medical Oncology (ESMO) [28]

[2]ASCO clinical practice guidelines [45]

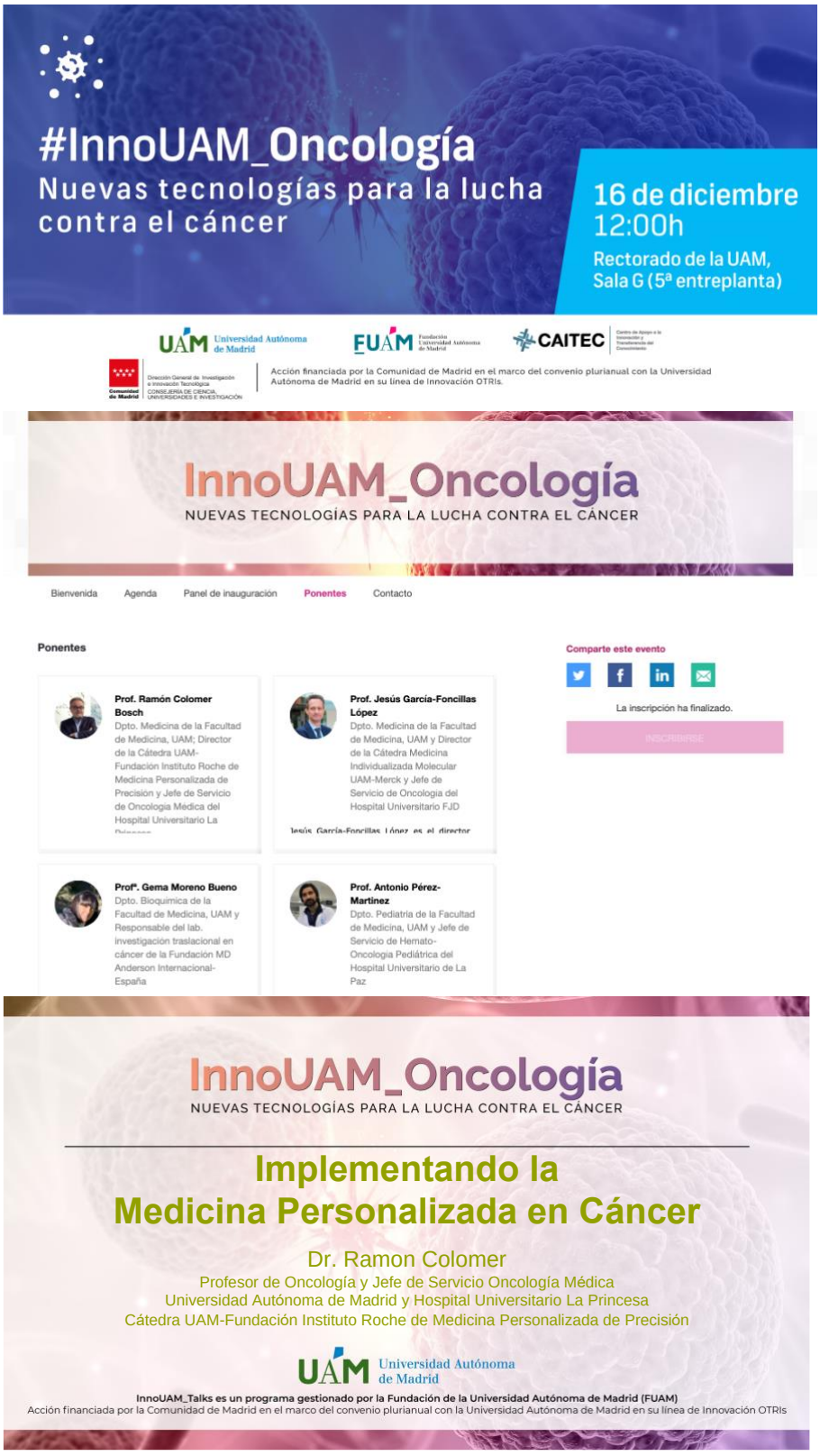
Difusión del Conocimiento

1. Creación de la App de la Cátedra de Medicina Personalizada de Precisión titulada Manual del Hospital la Princesa para Residentes de Oncología Médica (ONCORAMA)"

La aplicación y la difusión de esta App para Android y Apple iOS se aprobarán en la Junta Directiva de la Sociedad Española de Oncología Médica en enero de 2023.

Se publicará la versión 2022.2

2. Participación en la Jornada InnoUAM_Oncología de Nuevas Tecnologías para la lucha contra el Cáncer (16 de diciembre de 2021)



3. Participación en el acto 20 Aniversario de las Cátedras UAM (7 de noviembre de 2022)

ÍNDICE DE CÁTEDRAS

FUAM

Cátedra UAM - Fundación Instituto Roche de Medicina Personalizada de Precisión

Creación: 26/04/2017
Director: Ramon Colomer Bosch y Francisco Sánchez Madrid.
Departamento: Medicina.
Centro: Facultad de Medicina.

Cátedra de Medicina Personalizada de Precisión

Objetivos:
Fomento de la docencia, la investigación y la difusión de los conocimientos en salud particularmente en lo referente a la Medicina Personalizada de Precisión

Actividades destacadas:

Difusión del Conocimiento:

- Comparecencia Parlamentaria, en la Ponencia de Estudio sobre Genómica. XII Legislatura, Senado de España, Madrid
- Conferencia Inaugural en el XXXIII Seminario Interdisciplinar de Bioética 2019: "*Bioética y Cáncer: Medicina de precisión en oncología: éxitos y perspectivas*".
- Foro Debate "*Las nuevas Terapias y la Medicina de Precisión: Avances y Desafíos del Nuevo Paradigma de la Sanidad del Siglo XXI*", Farmaindustria - El Español, Madrid.
- Conferencia "*Medicina Personalizada de Precisión*", en #InnoUAM_MedicinaPersonalizada.
- Publicación de artículo de Opinión en Gaceta Médica. "2020: Un nuevo modelo de Oncología de Precisión"
- Publicación de una entrevista y video-entrevista en **Redacción Médica 13/01/2020**
- Conferencia Científica "Medicina Personalizada, de la Ilusión a la Precisión". Academia Nacional de Medicina de México.
- Publicación de una video-entrevista sobre Medicina Personalizada de Precisión en Univadis de Medscape.

Producción Científica:

- Publicación del artículo científico "*When should we order a Next Generation Sequencing test in a patient with cancer*".
- Redacción del artículo científico "*Consensus Statement Multidisciplinary consensus on optimizing the detection of NTRK gene alterations in tumours*".
- Redacción del artículo científico "*Consensus of experts from the Spanish Pharmacogenetics and Pharmacogenomics Society and the Spanish Society of Medical Oncology for the genotyping of DPYD in cancer patients who are candidates for treatment with fluoropyrimidines*".
- Publicación del artículo científico "*FGFR1 amplification or overexpression and hormonal resistance in luminal breast cancer: rationale for a triple blockade of ER, CDK4/6, and FGFR1*".

Formación:

- Realización del Módulo de Medicina de Precisión del Máster de Oncología de la Sociedad Española de Oncología Médica SEOM.
- Seminario formativo para Médicos Generales - SEMERGEN: *I Ciclo de Conferencias Online en Medicina de Precisión para médicos de cabecera.*

FUAM

- Publicación online de las **Fichas de Oncología Personalizada**

Miembros del equipo de la Cátedra:

- Ramon Colomer Bosch.
- Francisco Sánchez Madrid.
- Rebeca Mondéjar Solís.
- Miguel Ángel Quintela Fandiño.
- Arantzazu Alfranca
- Mar Llamas

Distribución de la actividad de la cátedra:

FUAM

4. Coordinación de la mesa de discusión "Redes oncológicas integradas europeas" (23 de noviembre de 2022)

En esta mesa se discutieron entre otros aspectos, la implantación de la Medicina Personalizada de Precisión en los distintas Redes Oncológicas de los participantes.

16:30-17:30 SESIÓN ESPECIAL: "Redes oncológicas integradas europeas"

Moderan

Jesús García-Foncillas. (Fundación Jiménez Díaz)
Ramón Colomer. (HU La Princesa)

Intervienen

Gianni D'Errico. (Toscana Life Sciences. Florencia. Italia)
Dirk Arnold. (Asklepios Tumor Centrum. Hamburgo. Alemania)
Julien Taieb. (Georges Pompidou European Hospital. Paris. Francia)
Luis Costa. (Hospital Santa María. Lisboa. Portugal)
Júlio Oliveira. (Instituto Português de Oncologia do Porto. Portugal)
Ulrik Lassen. (Rigshospitalet. Copenhage. Dinamarca)
Pierre Laurent Puig. (Descartes Medical School. Paris. Francia)
Albrecht Stenzinger. (Universidad de Heildelberg. Heildelberg. Alemania)
Bernard Avouac. (Universidad de Lieja. Lieja. Bélgica)

Formación

1. Dirección del Curso online "Tumor Agnostic Academy", de 6 ECTS, en la UAH

Este curso ha tenido tres ediciones en 2022.

Formación Competencias Recursos formativos

Formación > **Tumour Agnostic Academy**

Tumour Agnostic Academy

Información

Curso online con 6 créditos ECTS de la Universidad de Alcalá de Henares sobre los nuevos avances en medicina de precisión, con foco en el abordaje tumor agnóstico. Principalmente dirigido a oncólogos médicos, oncopediatras, patólogos, biólogos moleculares y farmacéuticos.

En un tiempo en el que hay depositadas grandes esperanzas en la medicina de precisión, las terapias tumor agnósticas han surgido como un nuevo y revolucionario enfoque para el tratamiento del cáncer. Estas terapias, dirigidas a alteraciones genéticas específicas, independientemente del lugar de origen del tumor, señalan un nuevo e importante paradigma en el manejo clínico de los pacientes. Debido al enorme interés que este nuevo abordaje terapéutico está generando, tanto para pacientes adultos como pediátricos, es esencial aumentar el conocimiento con una perspectiva multidisciplinar, desde el diagnóstico hasta el tratamiento, así como de los aspectos farmacoeconómicos asociados a este tipo de terapias. Con este propósito se pone en marcha el Curso de Formación online "Tumour Agnostic Academy", con un formato atractivo, flexible y compatible con la labor asistencial de los profesionales clínicos.

Esta actividad tiene carácter de curso propio de formación continuada (Universidad de Alcalá, Madrid) acreditada con 6 ECTS (European Credit Transfer System). Los créditos obtenidos en estas Jornadas de la Universidad de Alcalá son reconocidos en cualquier universidad europea y se incluyen en el currículo como formación universitaria.

Estado
En curso

Modalidad
Online

Duración
1ª edición: Fecha de término: 15 julio 2022
2ª edición: Fecha de término: 5 septiembre 2022
3ª edición: Fecha de término: 28 octubre 2022

Fecha inicio
10/11/2021

Fecha fin
10/05/2022

Número de créditos
6 créditos ECTS.

2. Convocatoria y concesión de la Beca SEOM 2022 a la mejor Tesis Doctoral sobre Medicina personalizada de Precisión (20 de octubre de 2022)

El Premio a la Tesis Doctoral de Medicina Personalizada de Precisión para Investigadores Jóvenes de SEOM galardona a la doctora Olga Martínez Sáez

La doctora Olga Martínez, oncóloga médica del Hospital Clínic de Barcelona; recibe el premio de manos de Ramón Colomer, profesor docente e investigador de la Facultad de Medicina de la Universidad Autónoma de Madrid (UAM); y de Enriqueta Felip, presidenta de SEOM.

24/10/2022

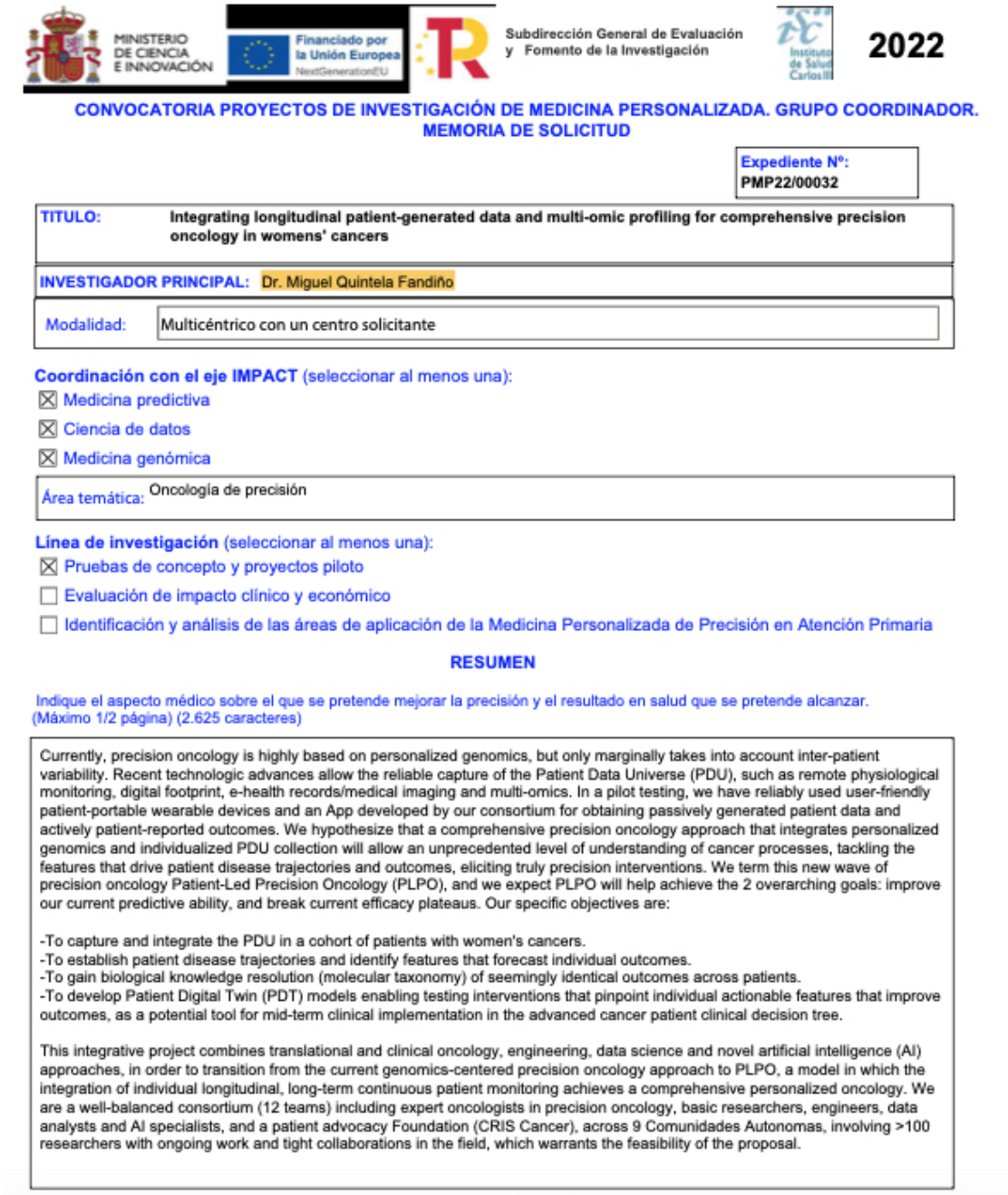
La doctora Olga Martínez Sáez, oncóloga médica del Hospital Clínic de Barcelona, es la ganadora del Premio a la Tesis Doctoral del Programa de Becas SEOM 2022 que está financiada por la Cátedra de Medicina Personalizada de Precisión de la Universidad Autónoma de Madrid - Fundación Instituto Roche, con una dotación de 3.000€.

Esta beca es una de las acciones impulsadas desde la Cátedra en el ámbito de la formación en Medicina Personalizada de Precisión. La Cátedra tiene el objetivo de anticipar los continuos avances que se están produciendo en el campo de la Medicina Personalizada de Precisión e impulsar el necesario debate público sobre aspectos específicos científicos, de política sanitaria, legislativos, regulatorios, éticos y económicos de la Medicina Personalizada de Precisión.

Así, tal y como ha afirmado **Ramon Colomer**, *profesor docente e investigador de la Facultad de Medicina de la Universidad Autónoma de Madrid* (UAM), "***la formación y la investigación son dos herramientas fundamentales en Medicina para lograr avances científicos y, por ello, desde la Cátedra apostamos por colaborar con los oncólogos que investigan académicamente en el campo de la Oncología y de la Medicina Personalizada de Precisión***".

Investigación

Concesión del Proyecto de Investigación titulado "Integrating longitudinal patient-generated data and multi-omic profiling for comprehensive precision oncology in womens' cancers" (Expediente No: PMP22/00032), dentro de la Convocatoria de Proyectos de Investigación de Medicina Personalizada del Instituto de Salud Carlos III.



MINISTERIO DE CIENCIA E INNOVACIÓN

Financiado por la Unión Europea NextGenerationEU

Subdirección General de Evaluación y Fomento de la Investigación

Instituto de Salud Carlos III

2022

CONVOCATORIA PROYECTOS DE INVESTIGACIÓN DE MEDICINA PERSONALIZADA. GRUPO COORDINADOR.
MEMORIA DE SOLICITUD

Expediente Nº: PMP22/00032

TITULO:	**Integrating longitudinal patient-generated data and multi-omic profiling for comprehensive precision oncology in womens' cancers**
INVESTIGADOR PRINCIPAL:	Dr. Miguel Quintela Fandiño
Modalidad:	Multicéntrico con un centro solicitante

Coordinación con el eje IMPACT (seleccionar al menos una):

☒ Medicina predictiva
☒ Ciencia de datos
☒ Medicina genómica

Área temática: Oncología de precisión

Línea de investigación (seleccionar al menos una):

☒ Pruebas de concepto y proyectos piloto
☐ Evaluación de impacto clínico y económico
☐ Identificación y análisis de las áreas de aplicación de la Medicina Personalizada de Precisión en Atención Primaria

RESUMEN

Indique el aspecto médico sobre el que se pretende mejorar la precisión y el resultado en salud que se pretende alcanzar. (Máximo 1/2 página) (2.625 caracteres)

Currently, precision oncology is highly based on personalized genomics, but only marginally takes into account inter-patient variability. Recent technologic advances allow the reliable capture of the Patient Data Universe (PDU), such as remote physiological monitoring, digital footprint, e-health records/medical imaging and multi-omics. In a pilot testing, we have reliably used user-friendly patient-portable wearable devices and an App developed by our consortium for obtaining passively generated patient data and actively patient-reported outcomes. We hypothesize that a comprehensive precision oncology approach that integrates personalized genomics and individualized PDU collection will allow an unprecedented level of understanding of cancer processes, tackling the features that drive patient disease trajectories and outcomes, eliciting truly precision interventions. We term this new wave of precision oncology Patient-Led Precision Oncology (PLPO), and we expect PLPO will help achieve the 2 overarching goals: improve our current predictive ability, and break current efficacy plateaus. Our specific objectives are:

-To capture and integrate the PDU in a cohort of patients with women's cancers.
-To establish patient disease trajectories and identify features that forecast individual outcomes.
-To gain biological knowledge resolution (molecular taxonomy) of seemingly identical outcomes across patients.
-To develop Patient Digital Twin (PDT) models enabling testing interventions that pinpoint individual actionable features that improve outcomes, as a potential tool for mid-term clinical implementation in the advanced cancer patient clinical decision tree.

This integrative project combines translational and clinical oncology, engineering, data science and novel artificial intelligence (AI) approaches, in order to transition from the current genomics-centered precision oncology approach to PLPO, a model in which the integration of individual longitudinal, long-term continuous patient monitoring achieves a comprehensive personalized oncology. We are a well-balanced consortium (12 teams) including expert oncologists in precision oncology, basic researchers, engineers, data analysts and AI specialists, and a patient advocacy Foundation (CRIS Cancer), across 9 Comunidades Autonomas, involving >100 researchers with ongoing work and tight collaborations in the field, which warrants the feasibility of the proposal.

Con este proyecto de investigación exploraremos los distintos aspectos de la Medicina Personalizada de Precisión de una manera integrada. La financiación concedida para el período 2023-2025 ha sido de 2.439.992,50 €. En este proyecto multicéntrico participan las siguientes instituciones:

PLPO Alliance groups

-Coordinating institution: CNIO – Clinical Research Program (**CRP**). -Artificial Intelligence and Data Science Consortium: it is formed by two groups: 1) Universidad Politécnica de Madrid – Laboratorio de Inteligencia Artificial (**AIL-UPM**) and Universidad Carlos III – Group de Procesamiento de Señales (**UC3M – SPG**).

-Clinical Consortium: 10 Institutos Sanitarios and Hospitals: Hospital La Princesa (**HLP**); Hospital Clinico de Valencia (**HCU-Val**); Complejo Hospitalario de Navarra (**CH-Nav**); Hospital Virgen de la Macarena (**HV- Mac**); Hospital Duran i Reynals (**ICO-Bell**), Hospital Central de Asturias (**HUCA**), Hospital San Pedro de Alcántara – Cáceres (**HSPC**), Complexo Hospitalario Universitario A Coruña (**CHUAC**) and Hospital Son Espases (**HSE**). The clinical activity of the CNIO oncologists takes place at the CNIO Unit at the Hospital de Fuenlabrada (**HFL-CNIO**).

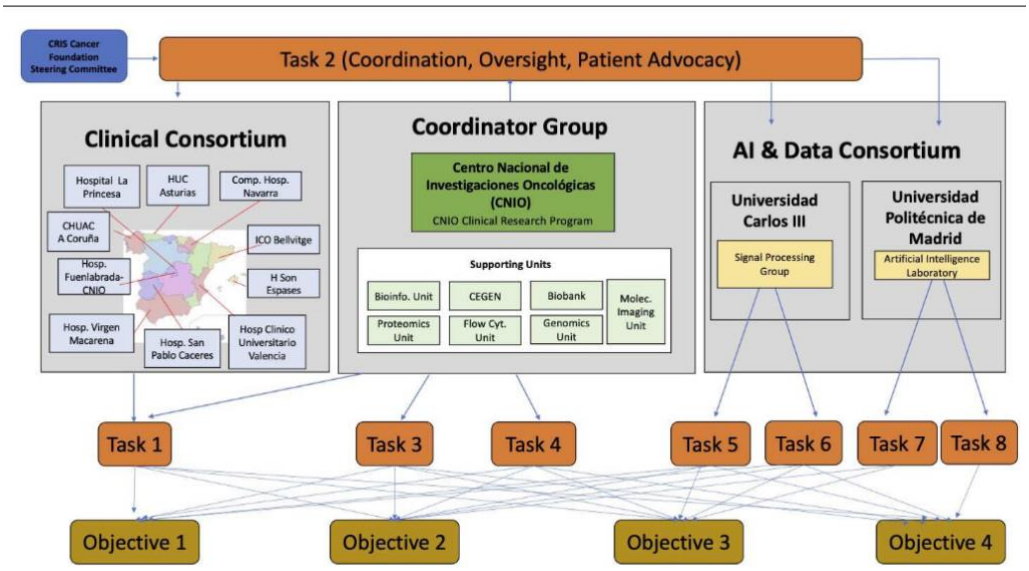
-Project management and coordination team: staff from the CRP.

-Patient advocacy group and oversight committee: CRIS Cancer Foundation will lead the steering committee

Aunque la Cátedra no percibe financiación específica, uno de los méritos considerados fue la participación del Director y uno de los Profesores Asociados de la Cátedra de Medicina Personalizada de Precisión en el proyecto. En el proyecto se hace constar la relación con la Cátedra:

Specific structures related with the focus of the Project

Dr. Miguel Quintela-Fandino, coordinator of the Project, and Dr. Ramon Colomer, and part of his team at the Hospital La Princesa, are associated with the Endowed Chair for Personalized and Precision Medicine at the Universidad Autónoma de Madrid since (associate professor and Director, respectively). This University Chair funded by the Fundacion Instituto Roche was created in 2017 to create knowledge in relation with Personalized Medicine, and the activities include the generation of oncology textbooks, national and international courses and meetings, or doctoral thesis.



Otras Actividades Relevantes en 2022

1. Incorporación al Grupo de Trabajo de la Sociedad Española de Oncología Médica (SEOM) de Medicina de Precisión

Medicina de Precisión - Observatorio

En SEOM consideramos prioritario avanzar en la implementación organizada de la Medicina de Precisión en Oncología y trabajaremos desde esta Comisión para que esto sea una realidad en el Sistema Nacional de Salud.

OBSERVATORIO Medicina de Precisión

- Mapa con respuestas por CCAA a la encuesta de SEOM sobre Medicina de Precisión *(acceso exclusivo a socios)*

Miembros de la Comisión

- Dra. Enriqueta Felip Font *(Coordinadora)*
- Dra. Pilar Garrido López *(Coordinadora)*
- Dr. Javier de Castro Carpeño
- Dr. Ramon Colomer i Bosch
- Dra. Carmen Esteban Esteban
- Dr. Juan de la Haba Rodríguez
- Dr. Antonio González Martín
- Dr. Rafael López López
- Dr. Aleix Prat Aparicio
- Dr. David Vicente Baz

Formación

- Jornada sobre Medicina de Precisión (16 de marzo de 2022)

Oncopodcast

30/03/2022

Dra. Enriqueta Felip y Dra. Pilar Garrido López: Medicina de Precisión, cómo organizarla e implementarla en España

2. Incorporación como coordinador en la Comisión de Becas y Premios de la Sociedad Española de Oncología Médica (SEOM)

Comisión SEOM de Becas

Las funciones básicas consisten en diseñar la convocatoria de becas (número, cuantía, categorías etc.) y fallar las becas basándose en las puntuaciones de los evaluadores externos.

Esta Comisión está compuesta por los siguientes doctores:

Dr. Ramón Colomer (Coordinador)
Hospital Universitario de la Princesa. Madrid

Dra. Carmen Riesco Martínez
Hospital Universitario 12 de Octubre. Madrid

Dr. Joan Brunet i Vidal
Hospital Universitari Dr. Josep Trueta. ICO Girona

Dr. César Serrano García
Hospital Universitario Vall D'Hebron. Barcelona

Dra. Enriqueta Felip
Hospital Universitario Vall D'Hebron. Barcelona

Dr. David Vicente Baz
Hospital Universitario Virgen Macarena. Sevilla

Dra. Tania Fleitas Kanonnikoff
Hospital Clínico Universitario de Valencia

3. Creación de la Unidad Funcional de Dermatooncología de Precisión en el Hospital de la Princesa de Madrid

Esta UF está formada por miembros de los Servicios de Dermatología, Oncología Médica, con la participación de radiología, Anatomía Patológica, entre otros.

Funciona desde septiembre de 2022, coordinada por los Dres Pedro Rodríguez Jiménes y Berta Hernández Marín.

PLAN DE ACTIVIDADES PARA EL AÑO 2023

1. Edición 2023 del Módulo de Medicina Personalizada de Precisión del Máster de Oncología Médica de la Sociedad Española de Oncología Médica (SEOM) y la Universitat de Girona.
2. Edición 2023 de las Fichas de Oncología Personalizada
3. Publicación de las *slide decks* de los Consensos de Biomarcadores realizados por la SEOM y la SEAP
4. Lectura de Tesis Doctoral Predictores de respuesta tratamiento con anticuerpos monoclonales frente al receptor de muerte programada (anti-PD-1) en paciente diagnosticados de cáncer de pulmón, Jacobo Rogado Revuelta, Matricula 10/2017, UAM.
5. Lectura de Tesis Doctoral Evolucion temporal del tratamiento neoadyuvante del cancer mama. Ana Isabel Ballesteros García, Matrícula: 10/2017, UAM
6. Lectura de Tesis Doctoral Análisis de supervivencia del cáncer colorrectal metastásico. Estudio retrospectivo de la vida real. Patricia Toquero Díez Matricula 11/2020, UAM
7. Lección opcional sobre MPP con formato de Seminario en la asignatura de Oncología impartida en la Unidad Docente de la UAM, en 2022.
8. Segunda edición del Premio a la mejor Tesis Doctoral de Medicina Personalizada de Precisión
9. Planificación de un Curso presencial de Medicina Personalizada de Precisión en el Centro Nacional de Investigaciones Oncológicas