Today's interview is with Dr. Ignacio Wistuba, Department Chair of the Department of Translational Molecular Pathology, Division of Pathology/Lab Medicine, and professor of the Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine, at The University of Texas MD Anderson Cancer Center.

Please tell us a little bit about the main focus and highlights of your research.

My research focuses mostly in the characterization of molecular abnormalities of lung cancer and its premalignant lesions to identify predictive biomarkers of response to novel therapies and early diagnosis of this disease. In the last two years, I have focused my research work on the analysis of immune response in lung cancer and other tumor types to identify predictive biomarkers for immunotherapy. Currently, I also dedicate a significant part of my time working on developing resources that enable translational and clinical research in a large number of tumor types.

The Origin Story

What are the discoveries that have lead up to your current work?

Early in my career, I contributed to the development of the “field of cancerization” concept in lung cancer by identifying that genomic allelic losses and instability occurred very early in the pathogenesis of lung cancer, involving histologically normal epithelium in tobacco smokers. Then, when I moved to MD Anderson in 2003, I developed a translational research program in lung cancer aiming to identify predictive biomarkers to precision medicine approaches. This program is the basis of our current TMP programmatic effort that expanded to other tumor types.

How did you come up with this hypothesis & what got you interested?

This is a hard question for me, since I do not consider myself a classic scientist, and formalizing hypotheses is not the way my mind works. I believe in exploratory work followed by good research practices. My earlier studies in lung premalignancy were based on the hypothesis that a widespread genomic damage must occur in the airway of smokers at high-risk to develop cancer. In this context, the key question revolved around identifying which lesions were associated with smokers who eventually progressed to develop invasive cancer. My current interest in clinical research of lung cancer and other tumor types is based on the hypothesis that precision medicine approaches, which avoid unnecessary toxicities, can be more effective to treat metastatic tumors than more conventional cytotoxic therapies.

What spurred this study or this question?

The increasing incidence of lung cancer in the USA and around the world, and our interest to develop clinically relevant markers for early diagnosis and identify targets for interception of premalignancy progression are key drivers for our continued work in this area. In the advanced metastatic lung cancer setting, the success of targeted and immune-based therapies has inspired others and me to work on this field of research.

So what?

Why is your research important? What are the possible real world applications?

As I stated, early detection of tumors is key to cure cancer, particularly lung malignancies, and targeted and immune-based therapies have shown to work to some extent in this and other diseases.

What kind of response have you gotten to your research / findings?
Most of my research has been translational, collaborative and multidisciplinary. I have been able to set up projects and approaches that are well accepted by collaborators from basic and clinical areas, and funding sources.

What challenges were you setting out to address when you started this work?

Personally, lack of formal research training has been a constant challenge to me. However, I have been fortunate to have great colleagues and mentors, and I have been able to work with great basic and clinical researchers from whom I have learned tremendously at MD Anderson and elsewhere.

Why were those important?

I believe that the lack of formal research training has been important to me because it instilled an obligation to work harder to be able to catch up and challenged me in being up-to-date in a rapid evolving field of research field.

Big picture: What’s your assessment of the current state of your research?

Translational research of cancer to identify markers for early detection and to predict response to novel therapies have shown to be successful to some extent in lung cancer, and it is leading the way in the oncology field. Personally, I am using my experience from lung cancer research and translate it to other tumor types.

Why is your area of scientific discovery relevant for ordinary citizens of this country?

Biomarkers to predict targeted therapy in lung cancer have shown to be effective in a major subtype of lung cancer, the adenocarcinoma histology, and immunotherapy has shown to be effective in a large subset of lung tumors overall. However, there is still a long way to go and to dramatically improve the survival of the large majority of lung cancer patients. Although a CT screening-based approach has shown to improve survival of smokers at high-risk to develop lung cancer, we are yet to identify good biomarkers to better screen subjects and to develop effective interception strategies.

What happens next in the process of discovery?

My research is close to clinical application, so that “next” step has been always critical for me. However, I think that cancer research should always aim for translation to the clinic as quickly as possible.

Light up the interview

What has been / was your most important scientific finding? Your most surprising finding?

Early in my career, the most important scientific finding was the identification of significant molecular aberrations happening in histologically normal airway epithelium of smokers and patients with lung cancer. This finding was confirmed 10 years later when I joined MD Anderson and our group determined for the first time that EGFR mutations are detected in the peripheral histologically normal airway epithelia of patients with EGFR-mutant lung adenocarcinomas.

Are your methods generally accepted? Are they unusual or novel?

I think so. As I work with clinically relevant human tumor tissues or cell specimens, usually very limited in quantity, I have faced some skepticism on whether comprehensive molecular or immune analysis can be
achieved using such small specimens. However, technologies have evolved and I have been fortunate to apply these to my research.

*Is there controversy in this area?*

Not much controversy, fortunately.

*What’s next?*

As I indicated, “next” in my research is always clinical application. Currently, I am working hard to continue the development of several programmatic efforts to significantly improve opportunities for translational and clinical research in our institution and other organizations. At MD Anderson, we are trying to improve our front-door collection of human specimens for research, continue the expansion of the longitudinal collection and profiling of specimens from patients enrolled in clinical trials through the Moon Shot APOLLO platform, and more recently, collaborating in the molecular characterization of rare tumors as part of our institutional Operational Priorities “Decisive Discoveries” and the Institute of Personalized Cancer Center (IPCT). At national level, I am leading a national effort to improve comprehensive immune and molecular profiling of specimens obtained in patients enrolled in immunotherapy trials in the NCI clinical trial networks through the CIMAC network.

**Personal details**

*Briefly, what most excites you about your work?*

Being involved in team and multidisciplinary-based research excites me every day. Although challenging, it is clearly a learning experience, and when it works, is very rewarding. In addition, having the privilege of leading the TMP team and assist to develop several institutional translational and clinical research programs is definitively very exciting!

*What hobbies do you have outside of research?*

I like very much to read. Since I was a young boy, I have been an avid reader. During the last 20 years, I have been reading mostly novels written by Latin American and Spanish authors. I take advantage of my travels to visit bookstores and buy books. I wish I would have more time to read! I also like movies, and I have special interest for classic art movies, a passion that I share with some of my daughters. But if I have to pick one hobby, I would pick spending time and playing with my two grandsons, Ayden (3 years old) and Wes (1 year old soon).

**Quirky details**

*What do you think is most interesting or coolest about your work?*

To work with a team of very dedicated and smart people, so I have the chance to learn every day!

*Do you have any entertaining story that you would like to share?*

I have several of course, I am old. However, I would like to mention some recent events that are rather sad, but involves very inspirational people. On late December 2018 and early January 2019, in a matter of 5 days, sadly, two of my dearest mentors, and giants of oncology, unexpectedly passed, Dr. Adi Gazdar (UT Southwestern Medical Center) and Dr. Waun Ki Hong (MD Anderson Cancer Center). It has been a very sad time for me and many others inspired by them, but personally, it has been extremely difficult since I had the fortune to be directly mentored and positively impacted by both of them. However, through these sad times, I have reflected a lot on the importance of relationships with those around you and about the value of mentorship and friendship. Having an impact on people in a positive manner is very valuable and meaningful.