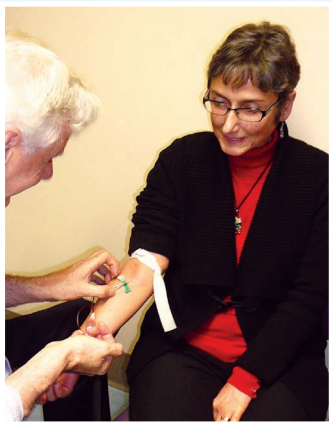
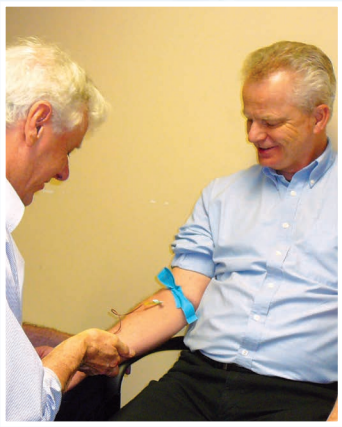
Spotlight on Research
SABC Research Program

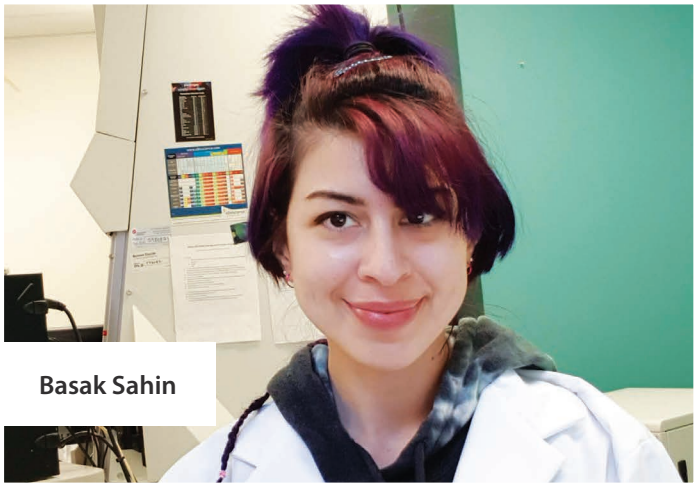
It was the summer of 2017 when many of us, patients and supporters alike, marched into the Scleroderma Clinic/Pacific Lung Health Centre on the 8th floor at St. Paul's hospital, rolled up our sleeves, and bared our arms to provide blood and skin samples. Some of us arrived at the clinic from all parts of B.C. as we know, Scleroderma is a rare disease with few specialists practicing in remote regions of the province. We signed-up to be participants in a Scleroderma research study titled Circulating and Cellular Biomarkers for Lung Disease in Systemic Sclerosis (SSc) and Idiopathic Pulmonary Fibrosis (IPF) or known to most of us as simply The Scleroderma Association of B.C. Research Project.

IT'S ALL ABOUT THE miRNAs

What we knew at the time of signing our consent forms and offering up our blood and skin is that the researchers would analyze our samples, looking for 'biomarkers' which are indicators of normal or abnormal biological processes or disease. Specifically, researchers would be assessing ribonucleic acid (RNA) which is the material that expresses DNA genes. Small sequences of RNAs, or microRNAs (miRNA), are vital in gene silencing, or the 'turning off' of gene expression. Because the levels of several miRNAs have been found to be abnormal in several conditions including SSc, researchers would be measuring the levels of miRNA sequences in our samples to identify if they are, in fact, potential biomarkers (predictors) of SSc and IPF. For example, if a patient's sample has a lower amount of a given miRNA sequence compared to a supporter's or 'control' sample, perhaps that low level is a biomarker or predictor for SSc. Discovering which miRNA sequences are too low or too high and correcting these imbalances could lead to effective treatment of skin damage in patients with Scleroderma and treatment of lung damage in patients with IPF only and in patients with both Scleroderma and IPF.







Basak Sahin

The SABC Research Project researchers are known to us all as Drs. Jim Dunne, Kevin Keen, Pierce Wilcox, Chris Ryerson and research coordinator Fran Schooley. **But there are many more experts, working behind the scenes on this project, analyzing our samples, collating the data and reporting out the results. One of these experts and the focus of this article is Basak Sahin**. Basak is a research technician at the Molecular Phenotyping Core of UBC Centre for Heart Lung Innovation at St. Paul's Hospital and has been with the SABC Research Project since the beginning. She works directly with Beth Whalen, the lab manager and supervisor and the two are each other's backup and support. Also on the research team is Iris Yao, this year's student who presents and reviews consent forms with study participants and Gurpreet Singhera who kindly volunteered to help with the western blot lab tests.

Basak's background is in molecular biology and genetics and she worked with small RNAs and nano/microparticles during her graduate studies. Basak became interested in working on the SABC Research Project while attending one of Dr. Dunne's infamous lab 'hurricane meetings', described as consisting of 15 minutes of brainstorming any number of different research ideas. Due to Jim's contagious enthusiasm (and long-standing relationship with the team at the Centre for Heart Lung Innovation), Basak joined the project in 2016, bringing with her the much-needed expertise for the start of the miRNA arm of the study.

SABC Research Program

Basak Sahin, Gurpreet Singhera and Beth Whalen

Speaking of enthusiasm, Basak is familiar with the SABC being the main source of support for this study, both financially and in terms of spreading the word. Basak has also joined Scleroderma patients, their friends and family members at the annual June fundraiser, SABC's Scleroderma Ride for Research in Stanley Park. The support for research certainly contributes to Basak's enjoyment in working on the project. In her own words, **"There is always something new and exciting happening".** She continues to be energized after Jim's research meetings, reading up and delving further into study ideas, pouring over spreadsheets, reviewing needed inventory and planning, planning, planning.

The SABC Research Project is just one of many projects Basak works on, though our study is the one she is most involved in. Basak's role in the project has involved the hands-on lab work in extracting the RNA from the blood and skin biopsy samples, preparing the extractions for sequencing and conducting the required lab tests. Basak also generates sheets of spreadsheet data that regularly end up in Dr. Keen's inbox, knowing he will make sense of them!

Basak explained in more detail exactly what has been happening with our samples. After collection at the clinic, the research team are called to pick-up the samples with instructions of which arm of the study the sample belongs to. Samples are coded with a unique ID to ensure patient confidentiality and the blood processed into different aliquots of plasma, serum, buffy coat and the RNA tube. The skin biopsy samples were used to grow fibroblast cells. Samples are continually stored until the researchers have enough patient and control samples to run a set of experiments.

Much work has gone into extracting and sequencing of RNA from the RNA tube aliquots and the fibroblasts grown out of the skin biopsies. Additional experiments include the use of qPCR and NanoString technology to validate the molecular signatures seen in the sequencing. Also performing ELISA, western blot and flow cytometry tests to identify and measure protein concentrations in the plasma and serum , even sending plasma samples to Dr. Martin Fritzler in Calgary to test for additional protein signatures.

She explains the research is really trying to figure out the pathogenesis or how the disease develops. Basak states, "**SSc can manifest in many different ways, causing different symptoms in different individuals seemingly without rhyme or reason. When that happens, it is hard to put your finger on a specific gene or pathway and say, hey this is where the problem is, lets fix that**. We know what happens, but we do not know why. We want to pinpoint the source(s) where things are going awry, because there is really very limited knowledge of Scleroderma.

We want to dive deep into the biology and figure out what exactly is going wrong to cause all the different symptoms. It is never a very viable option to keep treating the symptoms and not the source itself. Treating the symptoms is maybe going to slow down the disease progression or make it more comfortable for the patients to live with it, but not stop or reverse the disease itself".

SABC Research Program

According to Basak, the main goal of the SABC Research Project is to understand how all these pathways are interacting to cause the multitude of results and to try and understand which proteins, RNAs and DNA interact to make this complex machinery work (or in some cases, not work). The team is hopeful they are on their way to identifying a pathway that may be one of the main culprits in the disease progression. Identification is the first step which leads to understanding which leads to maybe one day, fixing it.

Basak continues with **"one of the things we think might be causing the disease and the variety of symptoms is an issue with cell to cell communication**. You have many different types of cells in your body, each with a different specialization. Cells need to 'talk' to one another to make this incredibly complex machinery that we call our bodies work properly. They achieve this communication by packing up and sending out 'envelopes' (called extracellular vesicles) to each other. Inside the envelopes are 'letters' consisting of proteins, RNA, DNA and most importantly for our research, miRNA, tiny RNA particles that carry information to regulate gene expression.

What happens when the cell is not able to pack the envelopes properly? When the letters inside are incomplete or different from what they need to be? We want to figure out which envelope is deficient or which cell type is having problems composing their letter. Then we can come up with a targeted strategy to fix the communication problem".

Basak mentions another goal of researching SSc is to be able to stratify patients into main and disease subgroups. Stratification will provide better, more personalized patient treatment for their specific prognosis. The preliminary research results do indicate a few molecular signatures may have been identified (validation of results pending). There are people that get interstitial lung disease (ILD) and those that do not, there are people who have a more diffuse disease and people whose symptoms are more limited. We want to know why this is and what makes people get such different prognoses.

We all know that understanding how a disease works leads to more precise treatments and cures. Adding to the existing knowledge base using basic science eventually leads to better therapies in the clinic for the patients.

Thank you so much Basak for being SABC's first Spotlighted Researcher!

MICHELE GERVAIS
Vice-President
Scleroderma Association of B.C.

FOR DOCTORS ONLY:

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