

1 **Title:** Working at a Cancer Research Laboratory as a Medical Student: Experience of an Indian Student
2 Studying Medicine in Russia

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Contributor Role	Role Definition	Authors					
		1	2	3	4	5	6
Conceptualization	Ideas; formulation or evolution of overarching research goals and aims.	X					
Data Curation	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse.	X					
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Writing Review & Editing	Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre- or post-publication stages.	X

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1. Opportunities and difficulties that international medical students face in this field of research

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Accepted, in-press

1 **ABSTRACT.**

2

3 Medical education is incomplete without any experience in medical research. In Russia, many international
4 students study medicine, and some of them indulge in research along with their teachers and supervisors in
5 different fields of medicine. Being one of such students, I narrated my experience of working at a cancer
6 research laboratory in a Russian university and discussed the opportunities and difficulties that an international
7 medical student might face while studying medicine and doing research simultaneously.

8

9 **Key Words:** Medical Student, Russia, Biomedical Research

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1 THE EXPERIENCE.

3 The Beginning of the Journey

4 Like most universities in Russia, Kazan State Medical University also has students' science society that gives
5 medical students their first exposure to research.¹ Dry-lab work and clinical research are promoted through this
6 system, as it is cost-effective and much easier to do. Also, the opportunities for dry-lab-based research in the
7 clinical field are much more compared to preclinical fields. On the other hand, in the departments of
8 biochemistry, microbiology, pharmacology, physiology, and pathology majority of work is based on wet-lab and
9 needs more resources. Thus, only a few exceptional students are taken into wet-lab-based work depending on
10 their performance in students' science society. I was lucky to be one of them.

11
12 My journey in cancer research started in November 2018 at the Department of General Pathology when I joined
13 the laboratory of Prof. Sergei Boichuk. He was then our teacher in Pathophysiology and was at that time
14 investigating the mechanism of imatinib resistance in Gastrointestinal Stromal Tumor (GIST) cells.² During the
15 introductory session in the laboratory, the first question that came to my mind was "How do these cancers get
16 resistant?" It was a difficult question to answer indeed and to try to find the answer, I knew I had to get involved
17 in the research. Initially, my task was to follow the senior research assistants to learn the protocols and
18 techniques. The most important thing to learn was how to culture and passage the cells in a sterile condition,
19 and how to treat the cells with the drug of choice. Apart from that, I also had to learn the protocols of western
20 blot, flow cytometry, immunofluorescence, and the use of pipets and various other tools used in the laboratory.

22 Difficulties to Overcome

23 Among many difficulties, the language barrier was the most arduous to overcome. I was the only international
24 student working in the laboratory along with a few other Russian students. The best way for me to interact with
25 the rest of the team was to speak and understand the Russian language. It was difficult in the beginning, as the
26 vocabulary that we use in day-to-day life in Russia or during clinical rotations in the hospital is vastly different
27 from what we use in the laboratory. The knowledge of the nuances of the language is also a key to establishing
28 good relations among colleagues. Thus, it took much longer for me to gain good working confidence and
29 establish communication with other members of the team. Nevertheless, all my seniors and colleagues helped
30 me in every possible way to acclimate me to their work culture.

31
32 Another issue was balancing my studies with my laboratory work, which was certainly an excruciating task. After
33 attending all classes and lectures, I could spare only two to three hours every day for my laboratory work. On
34 some occasions, I could assist a senior in his work, while on the other occasions I would apprentice whoever
35 was available. It was difficult to synchronize with the work schedule of the senior research assistants as their
36 time was limited and so what should have taken a month to learn, took much longer. Sometimes I had to make
37 a choice, either to study for tomorrow's topic or to stay in the laboratory to learn the protocols. Often, I choose
38 the latter. This consequently had a bearing on my class rating. However, looking at the possible prospects, it
39 was a price I was willing to pay.

41 Attending Conferences

1 Assisting others in their work was my only contribution during the first year. By this time, although I had learned
2 most of the protocols and already knew how to use different equipment, I was still sitting idle. This was due to
3 the preallocation of project assignments and the absence of any new tasks in the laboratory. Thus, I requested
4 my supervisor to allow me to submit the research results to international conferences, for which I already had
5 the necessary experience. After due diligence, we decided to submit the research result at the 12th Annual
6 Meeting of the Korean Society of Medical Oncology.³ The submission process was easy enough, and the
7 research was accepted for a poster presentation, but arranging to visit the conference proved to be a tedious
8 task. Finally, with financial support from the University, I attended the conference in Seoul, Korea. The
9 conference was held for two days, 7-8 November 2019, from dawn to dusk. I have never attended a conference
10 of this magnitude with so many speakers and participants from all around the world. Among the speakers, the
11 most prominent name was Dr. William G. Kaelin Jr., Nobel Prize Laureate in Physiology or Medicine 2019. His
12 presentation on 'The VHL tumor suppressor gene: Insights into oxygen sensing and cancer' provided an in-
13 depth understanding of the oxygen sensing mechanism of cells and its implication in renal cell carcinoma. It
14 was indeed an overwhelming experience to meet so many great minds in just one place.

15
16 Soon after my return from Seoul, I decided to send our research data to another conference in Cambridge, UK.
17 It was much smaller in scale and meant for medical students only, so I expected to meet new contacts and get
18 acquainted with other like-minded students. The second UK-Russia Young Medics Conference was held on 6-
19 7th January 2020, and it gave me an insight into the work culture, lifestyle, and social values of the people of
20 the UK. I presented our findings on the combined effect of BGJ398 and Doxorubicin on the Imatinib-resistant
21 GIST.⁴ Although doctors and oncologists present there found the results interesting, they also criticized the
22 results because Doxorubicin is not normally used for treating GIST. From the discussion, I understood that all
23 results that are found to be useful preclinically, may not always be translated to the clinical arena. This was a
24 critical lesson for me.

26 **The Pandemic**

27 Upon my return, I reported to my supervisor and asked if I can join any project. About this time, a new project
28 was opened to investigate the resistance mechanism of GIST430 cells, and I was assigned to it. The initial
29 results of the projects were published at the 94th International Student Scientific and Practical Conference at
30 the VII International Youth Scientific Medical Forum "White flowers".⁵ But, soon after the project initiated, the
31 lockdown was imposed all over Russia in response to the COVID-19 pandemic. Work in the laboratory was
32 halted and so did our project. Only a few necessary experiments were running, and people at the laboratory
33 were working in small shifts. Students were barred from visiting the University for safety reasons, thus
34 preventing me from working in the laboratory. We could only attend our lectures and classes online and leave
35 the hostel on weekends, that too only for three hours to buy the necessary commodities. Life had come to a
36 standstill for six months. Meanwhile, I started working on a different project which was more statistical and can
37 be done easily at home. This project focused on the correlation of spice intake with colorectal cancer, and by
38 using international databases we found a significant correlation between these two. This almost took four
39 months for me to prepare the paper and was finally published in the International Journal of Medical students.⁶

41 **Failure and Success**

1 It was only in September 2020, once the lockdown had been lifted, that I visited the department to start the
2 pending project. Our lectures were still being conducted online, so I could give more time to my experiments
3 than before. I had to culture the cells, treat them with proper chemical agents, lyse them and conduct Western
4 blotting to find the target proteins. We propose a few hypotheses to describe the resistance mechanism of
5 GIST430 cells. For the next five months, we tested them at multiple attempts in different experiments. However,
6 unfortunately, every single experiment produced negative results, even after ruling out confounders. This back-
7 to-back failure was difficult to deal with; every time the experimental results came out negative, my self-esteem
8 went down. At one point I started doubting myself. I had to accept the harsh truth about research; that failure is
9 more common than success. After getting only negative results for five months, we decided to shut down the
10 project and move on.

11
12 Soon after that, I joined another project with a colleague who was working with triple-negative breast cancer
13 (TNBC) at the same laboratory. This was a new beginning for me. We were investigating the activity of a targeted
14 drug named Infigratinib on the TNBC cell line. During this project, time management became a difficult issue.
15 Because I not only had to work on my research and classwork but also had to prepare for the Indian screening
16 exam (FMGE) which is mandatory to pass to get a license to practice in India. This made life even harder, some
17 days I had to leave my room at 8 in the morning only to return at 11 pm after attending classes, lectures, and
18 lab work; then I had to cook, eat, and study for the next day until 2 am only to wake up next morning to repeat
19 the same routine. After almost seven months of rigorous investigation, we finally had some fruitful results. We
20 found that Infigratinib also targets p-glycoproteins in taxol-resistant triple-negative breast cancer cells and
21 synergizes with Paclitaxel, increasing its lethality. Indeed, this finding was a moment of joy for us. Finally, the
22 data from this project got published in March 2022.⁷

23 24 **Lessons to Learn**

25 Without any doubt, all the hardships that I went through taught me lessons that I could not learn any other way.
26 The first lesson was to be ready to accept any adversities that may come on the way. Learning to accept failure
27 is the key. Secondly, an aspirant must be ambitious, and with the help from an experienced supervisor, this
28 ambition will bear fruit. Thus, having a good supervisor who would support you even in difficult time is crucial.
29 Thirdly, exposure is necessary, and conferences not only allow us to learn about the current advancements in
30 research but also provide us with the necessary networking opportunities. Moreover, one must learn to ask for
31 help when needed, because research is a team effort and without help, one cannot get too far. Lastly, the
32 science and the experimental methods used in the research are difficult and can overwhelm anyone exposed
33 to them for the first time. Thus, one must be resilient and give an ample amount of time to understand it. Those
34 who do tend to stay in the research field for the rest of their life, while others find it difficult and leave. Research
35 is for those who are madly enthused about it. It takes a lifetime to be a scientist; there is a beginning but no end.

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1 FIGURES AND TABLES.

2

3 Figure 1. Digital poster presentation at KSMO 2019 International Conference, Seoul, Korea.

4

Inhibition of FGFR-signalling pathway modulates sensitivity of gastrointestinal stromal tumors to imatinib

Introduction
The acquired resistance of gastrointestinal stromal tumors (GISTs) to the imatinib (IM)-based targeted therapy remains the main driving force to find out the novel signaling pathways and approaches that are capable to re-sensitize GISTs to this therapeutic regimen.

Conclusion
Our data illustrates that inhibition of FGFR- signaling might be considered as a perspective molecular target to overcome GIST resistance to IM. Therefore, this type of the combined therapy might be effective for the patients with unresectable and metastatic forms of GISTs.

Methods and Materials
IM-resistant GIST T-1 cells were cultured with IM, FGFR inhibitor BGJ398 alone or in combination. GISTs viability and growth kinetics were analysed using MTS-based assay and iCELLigence system, respectively. Protein expression and apoptotic markers was examined by western blotting. Efficacy of BGJ398 was studied in vitro and in vivo.

FGF/FGFR expression in naive and IM resistant GIST-T1 cells

Result of FGFR signaling inhibition in naive and IM resistant GIST-T1 cells

In vitro and In vivo results of FGFR signaling inhibition in IM resistant GIST-T1 cells

Citation
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