



# **APEX 5 – Altitude Research Expedition**

## Huayna Potosí, Bolivia (4,700m) – June 2017

# **Expedition Report**



THE UNIVERSITY of EDINBURGH

#### Name of Expedition: APEX 5

#### **Expedition Contact Details:**

Email: <u>apex5@altitude.org</u> Website: <u>http://www.altitude.org/apex5.php</u> Facebook: https://www.facebook.com/APEX5expedition/

#### Expedition Leader/Organiser: Christopher Graham

Address: 60/9 Ratcliffe Terrace, Edinburgh, EH9 1ST Mobile: 07856441228 E-mail address: <u>apex5@altitude.org</u> or <u>christopherjgraham@hotmail.co.uk</u>

MEF Reference: 17-20

Country/Region: Bolivia / Huayna Potosí, Cordillera Real

With grateful thanks to:



Report author: Christopher Graham, contact details as above.

The Report was approved and edited by the APEX 5 organising committee, first published in October 2017, and updated in January 2018.

## Contents

Abstract	Page 4
Resumen (español)	Pages 5-6
Introduction	Page 7
Location maps and images	Pages 8-9
Expedition Members	Page 10
Activities and accomplishments	Page 11
Administration and logistics	Pages 12-16
<ul> <li>Guide to area and local information</li> <li>Research equipment</li> <li>Permission and permits</li> <li>Fundraising and finances</li> <li>Insurance</li> <li>Travel and transport</li> <li>Food and accommodation</li> <li>Communications</li> <li>Risks and hazards</li> <li>Injury and illness</li> <li>Medical arrangements</li> <li>Waste disposal</li> </ul>	
Research objectives	Pages 17-18
Expedition dates and research itinerary	Page 19
Next steps	Page 20
Conclusion	Page 21
Acknowledgments	Pages 22-23

### Abstract

#### Aims and objectives

Low oxygen levels (hypoxia) pose a significant physiological challenge to the human body. We aimed to collect physiological, psychological and genetic data from young healthy volunteers at sea level and at both moderate and high altitude in order to gain an insight into the human physiological response to hypoxia. Hypoxia is a feature of several medical conditions such as asthma and chronic obstructive pulmonary disease, and is common in intensive care patients. We hope that our research could lead to better treatment options for patients with low blood oxygen concentrations at sea level. Alongside this, we aimed to inspire and develop the next generation of clinical academics by providing a safe, well-organised, and rewarding research expedition to student volunteers.

#### Methodology

Our expedition took place between 19<sup>th</sup>-30<sup>th</sup> June 2017 in Bolivia. We acclimatised in La Paz (3,600m) for four days before ascending to Huayna Potosi base camp (4,700m) from day five until the end of the expedition at day twelve. Blood samples were obtained on day six and eleven to measure white blood cell gene expression and protein expression; to analyse the mechanism of platelet activation (a blood cell involved in clotting); and the effect of genetic variants known as eQTLs on gene expression. We also performed eye imaging, eye movement tasks and visual function tests on days six, eight and ten. All participants completed daily altitude symptom questionnaires. Participants also completed a personality trait questionnaire pre-expedition (the Neo Five-Factor Inventory), to evaluate if certain traits impact on how sick people feel at altitude. Baseline measurements for all studies were performed before the expedition in April 2017, whilst further blood samples were taken post-expedition to analyse white blood cell gene expression.

#### Results

Analysis and interpretation of our results are on-going. We aim to present and publish our research findings in due course.

#### **Discussion and Conclusion**

Snow and ice made access to Chacaltaya Mountain (our planned research location) impassable and therefore unsafe in case of evacuation due to health concerns. We relocated our research to Huayna Potosí base camp, thanks to excellent teamwork and quick thinking. Despite this set back, the expedition was a huge success, and we collected all data as planned. Data analysis is currently in progress. We look forward to completing analysis, disseminating our findings, and inspiring students to get involved in research and to consider organising APEX 6.

## **Resumen (español)**

#### Fines y objetivos

Niveles bajos de oxigeno (hipoxia) crean un gran desafío fisiológico para el cuerpo humano. Tuvimos la intención de obtener datos fisiológicos, psicológicos y genéticos de voluntarios jóvenes y sanos al nivel del mar y ambas a la media y a la alta altitud para obtener un conocimiento de la respuesta fisiológica humana a hipoxia. Hipoxia es una característica que existe en muchas condiciones médicas como el asma y la enfermedad pulmonar obstructiva crónica, y es común en pacientes de cuidados intensivos. Esperamos que nuestras investigaciones pudieran dirigir a opciones de mejores tratamientos para las pacientes con concentraciones sanguíneas bajas de oxigeno al nivel del mar. Adicionalmente, tuvimos la intención de inspirar y desarrollar la generación siguiente de académicas clínicas por proporcionar una expedición de investigaciones segura, bien organizada y gratificante para voluntarios universitarios.

#### Metodología

Nuestra expedición tuvo lugar entre 19 a 30 de junio 2017 en Bolivia. Nos aclimatamos en La Paz (3.600m) por cuatro días antes de ascender al campamento base de la Montaña Huayna Potosí (4.700m). Desde el día cinco hasta el fin de la expedición, día doce, trabajábamos en el refugio al base de Huayna Potosí. Muestras de sangre fueron obtenidas los días seis y once para medir la expresión genética y proteínica de células blancas; para analizar el proceso de la activación de células plaquetas (un tipo de célula sanguínea involucrado con la coagulación); y el efecto de variantes genéticos que se llaman eQTLs sobre la expresión genética. También, realizamos imágenes de los ojos, pruebas de movimientos oculares y pruebas de la visión en los días 6, 8 y 10. Todos los participantes completaron cuestionarios diarios de síntomas de la altitud. Los participantes también completaron un cuestionario antes de la expedición (Neo Five-Factor Inventory) para evaluar si tratos de personalidad afectan cómo la gente se siente en la altitud. Medidas de referencia para todos los estudios fueron realizados en abril 2017, y muestras de sangre adicionales fueron tomados después de la expedición para analizar la expresión genética de las células blancas.

#### Resultados

El análisis e interpretación de nuestros resultados están en marcha. Aspiramos a presentar y publicar nuestros resultados de investigaciones en un futuro cercano.

#### Discusión y conclusión

Nieve e hielo hicieron que el acceso a la Montaña Chacaltaya (nuestra ubicación planificada de investigaciones) fue infranqueable y por lo tanto inseguro en caso de evacuación por preocupaciones de salud. Nos trasladaron nuestras investigaciones al campamento base de la Montaña Huayna Potosí, gracias a trabajo de equipo excelente y la rapidez de reflejos. A pesar de este problema, la expedición fue un gran éxito, y colectamos todos los datos como planificado. El análisis está en marcha. Ansiamos completar el análisis, compartir nuestros resultados, e inspirar estudiantes a involucrarse en las investigaciones y considerar organizar APEX 6.

### Introduction

#### Background information to APEX 5

APEX (Altitude Physiology EXpeditions) is a charity based in Edinburgh, which aims to perform high altitude medical research and educate the public about altitude illness (Registered Charity: SC030345). Kenneth Baillie, who led the first APEX expedition to Bolivia as an undergraduate medical student, founded the charity in 2001.

The APEX 5 expedition was organised by six University of Edinburgh undergraduate medical students, with guidance and advice from Dr Kenneth Baillie and Dr Roger Thompson (both previous APEX Expedition Leaders). We were assisted with our research by a University of Edinburgh PhD student, Joseph Willson. Our research participants consisted of 27 University of Edinburgh students. Two members of the organising committee also acted as research participants.

The expedition was the sixth carried out by the APEX group, and the fifth to travel to Bolivia, South America.

The APEX 5 expedition builds on findings from APEX 4, the previous APEX expedition, as well as exploring new areas of research.

It is known that hypoxia (low oxygen) causes platelets to become more active and likely to aggregate – a key step in blood clot formation. Research from the previous APEX 4 expedition highlighted the role of a particular signalling pathway in this process. We explored this pathway in greater depth.

In addition, we have explored the effects of altitude on the immune system, vision and the eye, cognitive function, and gene expression. We also explored the interplay between psychology and symptomatology of altitude illness.

Our planned base for research, an unused ski lodge on Chacaltaya Mountain (5,300m), was inaccessible due to snow and ice. Road access is essential in case of altitude illness (for which rapid descent is the best, and only definitive, treatment) or another emergency, to allow safe return to the city of La Paz. We therefore relocated our research to nearby Huayna Potosí Mountain (4,700m). We were able to complete our planned research at this new location.

The APEX 5 expedition aimed to further broaden our understanding of the impact of hypoxia on the human body, with the ultimate aim of applying this knowledge to the treatment of hypoxic patients at sea level.

## Location maps and images



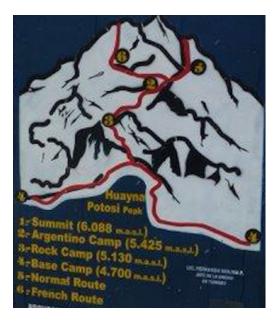


The APEX 5 team, with our volunteers, doctors, cooks, hostess, one of our drivers, and our adopted canine friends, outside our refuge at 4,700m.



The organising committee with Huayna Potosí as a backdrop.

Left-right: Gordon Paterson, Eleanor Lee, Jason Young, Greig Torpey, Rebecca Dru, Christopher Graham (and Joseph Willson, PhD student)



Our refuge was situated at point 4 (bottom right) where we performed all of our research and were based for the high altitude period of the expedition.



Huayna Potosí Glacier (and the expedition team) – for future reference, to evaluate the impact of climate change on this glacier.

## **Expedition Members**

#### **Organising Committee**

Christopher Graham	Expedition Leader and Research Lead
Rebecca Dru	Fundraising Coordinator and Deputy Expedition Leader
Greig Torpey	Logistics Coordinator and Research Lead
Jason Young	Research Lead
Gordon Paterson	Research Lead
Eleanor Lee	Volunteer Coordinator
Joseph Willson	PhD student and Researcher

#### **Expedition Doctors**

Ailsa Stott	General Practitioner
Nick Haslam	Acute Care Common Stem Trainee

#### **Expedition Members: Our Research Participants**

Ed McKee, Georgie Lewis, Jack Bayram, George Menon, Katie Gledhill, Abi Hosier, William Harper-Lawrence, Georgie Taylor, Georgia Gilbert, Eilidh Clark, Anna Kennedy, Sophie Hattersley, Rebecca Trimble, Scott Griffin, Erin Bennett, Alastair Woodhead, Eleanor Dewhurst, Denisa Stroncekova, Oscar Maltby, Shona Hutton, Colm Kennedy, Kate Johnson, Cathy Kitchen, Oliver Vick, Becky Price, Sarah Lewis, Catherine Lomax. Eleanor Lee and Rebecca Dru also acted as research participants.

We benefitted from the expertise of local mountain guide Marco Soria, whom we employed to assist with in-country logistics. Mr Soria organised cooks, meals, drinking water, drivers and vehicles.

## Activities and accomplishments

The expedition was an incredible experience for all.

For the organising committee, the expedition represented over two years of work and effort, culminating in the expedition itself. As a result of excellent teamwork, the expedition was a huge success despite a number of challenges, including the relocation of our research base.

The expedition was also a valuable experience for the research participants, all of whom were University of Edinburgh undergraduate students. We encouraged our student volunteers to ask questions and get involved in our research. For example, we organised half-day 'lab internships' to allow our volunteers to assist with the immunology and blood coagulation studies and learn how to process and prepare blood samples for analysis. These skills can be employed in many of the medical students' intercalated degree projects, and was reported to be a highlight for many volunteers. Students were also active participants in the eye research, imaging their own eyes and in the process learning ocular anatomy.

There were plenty of opportunities for expedition members to explore the stunning surroundings of Huayna Potosí. We enjoyed a team hike to the Huayna Potosí Glacier, as well as smaller group hikes to nearby lakes.

We made use of the opportunity to travel in South America following the expedition – members of the expedition team explored Bolivia, Peru, Chile, and Ecuador. Activities carried out after the expedition included summiting Huayna Potosí Mountain (Bolivia, 6,088m) and Yanapaccha Mountain (Peru, 5,460m), downhill mountain biking, land rover tours of the Uyuni Salt Flats, and exploring the Amazon Rainforest.

## Administration and logistics

#### Guide to area and local information

The refuge on Huayna Potosí provided the ideal venue to meet our specific research needs. We required safe and secure accommodation at high altitude, with easy access by road.

The weather was fine on most days.

Google Earth accuracy of the area is reasonable.

Future visitors should note that we were warned that robbery on the roads between Huayna Potosí and La Paz occurs not infrequently. There is a police checkpoint, but the threat remains. Visitors should avoid driving at night, where possible.

Visitors should also note that phone signal coverage is poor – ask local guides for advice on coverage (high quality reception was available a 30-minute drive from the refuge), and consider a satellite phone.

#### Research equipment used

Immune system research	2 x Hettich EBA 280 centrifuges, 2 x EasySep Magnets, Microscope, P20, P100 and P1000 pipettes, 2 x PIPETBOY, 1 microcentrifuge
Blood coagulation research	2 x Hettich EBA 280 centrifuges, 1 x QInstruments BioShake IQ, 1 x BMG LabTech SPECTROstar Nano, 1 x Vortexer
Macular function research	myVisionTrack <sup>®</sup> (mVT <sup>®</sup> ) App, Peek Vision Acuity App
Saccadic performance research	Ober Consulting Saccadometer
Fundus imaging research	Epipole EpiCam M, Epipole EpiCam C
Psychology research	Neo Five Factor Inventory, AMS Severity Questionnaire

#### Research equipment training

Gordon Paterson was trained in the use of the Hettich centrifuge by Mr Andrew Allison, a representative of the company. Additionally, he was trained in the usage of the SPECTROstar Nano by representatives of BMG LabTech. Extensive technical assistance with the research protocol was provided by the Warner research lab of Barts and The London School of Medicine and Dentistry

Jason Young was also trained in the use of the Hettich centrifuge by Mr Andrew Allison. He received training in the protocol for neutrophil isolation from whole blood by Joseph Willson (PhD student and APEX 5 Researcher) and Patricia Dos Santos Coelho.

Christopher Graham was trained in use of the Saccadometer by Ian MacCormick, an ophthalmologist and APEX 5 research supervisor. Both Eleanor Lee and Christopher Graham received training on the use of the Epipole cameras by the Epipole team, based in Rosyth, Scotland.

#### Permission and permits

No permits or permissions were required, however the British Embassy in La Paz wrote to the Bolivian Ministry of Foreign Affairs, the National Academy of Sciences of Bolivia, and the Instituto Boliviano de Biología de Altura, to notify them of our expedition.

We had no issues at customs on entry to Bolivia, but came prepared with letters from the University of Edinburgh, and from companies that loaned research equipment, to explain the purpose of our expedition. We also brought the Bolivian Ministry of Foreign Affairs customs approval letter with us.

We required approval from INLASA (Instituto Nacional de Laboratorios de Salud) to allow export of our biological samples. We arranged for CDC approval due to sample transit through the United States via our courier, World Courier.

#### Fundraising and finances

We opened an APEX 5 Royal Bank of Scotland Business Account.

We received grants from several funding bodies, as well as financial support from several sponsors. Details of these can be found in the budget (available on request) and acknowledgements section of this report.

We used a combination of Western Union transfer and cards (Revolut, Monzo, and a traditional bank card) in-country. We withdrew cash in Bolivianos (local currency) if necessary, but were wary of carrying too much money in case of theft, and distributed it between the organising committee where practical.

#### Insurance

Expedition members were required to provide written evidence of their travel insurance, including coverage for high altitude. The expedition doctors had appropriate medical indemnity cover. Our research equipment and the expedition as a whole were covered by University of Edinburgh policies, via ACCORD (Academic and Clinical Central Office for Research and Development) who granted ethical approval.

#### Travel and transport

Flights for expedition members were co-ordinated to arrive in La Paz within a 12-hour window to minimise any confounding effects of length of exposure to altitude on the studies.

Our research equipment was transported as (excess) baggage on our flights. In La Paz, we used taxis to travel with equipment, such as when charging the dry shipper with liquid nitrogen.

We hired buses to take the team and the research equipment to Huayna Potosí. In addition, we hired two four-wheel drive vehicles with drivers for the duration of the expedition in case of evacuation from the refuge in the event of emergency.

We employed World Courier to return our samples to the United Kingdom. World Courier has no local office, so we also worked with the local company Inbolcargo SRL.

#### Food and accommodation

Food was bought locally and prepared on site by a team of local cooks, who resided at the high altitude refuge during our stay. The food was of a high standard. We emphasised the importance of hand hygiene to the staff and volunteers, providing bottled water, soap, and alcohol gel. This minimised the incidence of gastroenteritis when compared to the previous APEX 4 expedition, a factor not only important for maintaining morale but also in minimising confounding in our research.

Marco Soria organised water – we bought clean, bottled water dispensers in bulk to minimise plastic waste. Empty bottles were collected and recycled by the water company.

Accommodation at Huayna Potosí was organised via Marco Soria and we paid the owner, Elvira in two instalments: on arrival and on departure. We stayed in the Hostal República (Calle Comercio, 1455) in La Paz for the four nights of acclimatisation prior to ascent, and on the last night of the expedition (June 30<sup>th</sup>).

#### Communications

The primary language spoken in Bolivia is Spanish. In addition, the Quechua and Aymara languages are spoken by indigenous people, sometimes exclusively. Rebecca Dru and Christopher Graham, who both had a good level of Spanish, acted as interpreters and translators, and facilitated much of the administrative work and in-country logistics. Other members of the organising committee and our volunteers had varying degrees of Spanish language ability. We encouraged our team to learn Spanish prior to the expedition using Duolingo and by providing a document of useful phrases/vocabulary.

Pre-expedition, the majority of our communication was via e-mail. We also communicated via Skype with our liquid nitrogen, dry ice and oxygen provider (Praxair, based in El Alto, La Paz), and the Instituto SELADIS haematology laboratory (of Universidad Mayor de San Andres, UMSA) with which we collaborated. Mail would not be effective (postcards took weeks-months to reach the UK).

We purchased four mobile telephones on arrival in La Paz. At least one was kept by the expedition doctors, and at least one by the organising committee. This enabled effective communication in La Paz, and

between the mountain range and La Paz (the most reliable signal was a 30-minute drive from the refuge, towards La Paz).

#### **Risks and hazards**

A full risk assessment was carried out prior to the expedition, reviewed by Dr Fanney Kristmundsdottir (Director of Medical Electives, University of Edinburgh) and approved by the University of Edinburgh's Expedition Committee. Ethical approval for the research was granted by ACCORD. Dr Matt Wilkes, an anaesthetist and APEX 4's expedition doctor, provided the expedition team with a talk on the risks and hazards of the expedition.

Our on-going risk assessment in country deemed Chacaltaya unsafe, and we therefore relocated to Huayna Potosí to ensure safe, rapid descent in case of emergency.

*Altitude illness:* Participants were fully informed of the potential negative consequences of exposure to high altitude. Common symptoms include shortness of breath, increased heart rate, headache, sleep disturbance, and reduced appetite. Rarely, it is also possible to develop oedema (fluid build-up) in the lungs and brain – High Altitude Pulmonary Edema (HAPE) and High Altitude Cerebral Edema (HACE), respectively. Although these conditions are serious, they usually resolve rapidly following descent and appropriate treatment.

*Other risks:* As with any form of travel, illness from poor hygiene was possible. We emphasised the importance of hand hygiene, including regular use of alcohol gel, and safe food and drink. We provided soap and alcohol gel at the refuge for all team members and our cooks, to whom we also emphasised the importance of hand hygiene. We provided clean, bottled drinking water to everyone. Accidents are a common cause of injury on an expedition, and in developing countries road traffic accidents are a significant risk. We provided advice on road safety, and ensured the vehicles we were using were appropriate and well-maintained. We also ensured the refuge was safe for our volunteers (taping electrical cables to the walls, for example). There was a small amount of risk associated with the research itself: this risk was carefully considered in terms of its implications for the safety of our volunteers, and all research was approved by the ACCORD ethical committee.

#### Injury and illness

Almost all members of the expedition experienced altitude illness of varying severity. No one had to be evacuated.

One expedition member fell and injured their hand, with no on-going problems. One expedition member had a period of severe nausea and vomiting, but this resolved. All health issues were reported to and dealt with promptly by our two expedition doctors.

#### Medical arrangements

We had two expedition doctors: Dr Ailsa Stott and Dr Nick Haslam.

Dr Nick Haslam was involved in the organisation and co-ordination of the expedition from an early stage, and instrumental in the pre-departure medical screening process and in creating our volunteer medical information pack. Dr Rhianwen Thomas, a General Practitioner, also assisted in the pre-departure medical screening process as our original second expedition doctor, but was unable to attend the expedition. We therefore recruited Dr Ailsa Stott, who demonstrated a wealth of experience in expedition medicine and was an asset to the expedition.

Dr Nick Haslam and Dr Ailsa Stott gave a medical briefing in La Paz early in the expedition.

Participants required vaccinations against Hepatitis A, Tetanus and Typhoid, and we strongly recommended the Yellow Fever vaccination. The Yellow Fever vaccination and certification was not required for entry to Bolivia, but guidance regarding this was conflicting. Malarial prophylaxis was recommended for those travelling below 2,500m following the end of the expedition. All volunteers were required to bring their own supply of essential medical equipment (painkillers, diarrhoea treatment, simple antibiotics, plasters, water purification tablets etc.) to supplement the medical team's own supply and prevent stock exhaustion.

We made arrangements with a local hospital (Clínica Alemana, Avenida 6 de Agosto, 2821, La Paz) in case any expedition members became unwell.

The organising committee and expedition doctors went through a 'mock' evacuation on our arrival to La Paz and again on arrival to the lodge at Huayna Potosí. The organising committee familiarised themselves with the medical kit and knew its whereabouts at all time. All volunteers were made aware of the doctors' hostel room numbers in La Paz, and their contact number.

#### Waste disposal

General waste was removed daily by the drivers, and disposed of appropriately in La Paz.

We took clinical waste bags and sharps disposal systems to Bolivia from the UK. Clinical waste and sharps were disposed of by SELADIS, the laboratory group in La Paz with whom we collaborated.

We used plumbed toilets on Huayna Potosí.

## **Research objectives**

Our main research question was: *How does gene expression in human leukocytes (and, specifically, neutrophils) change in response to a prolonged exposure of low oxygen levels (hypoxia)?* 

Specifically, we were interested in whether a period of prolonged hypoxia affects gene expression of new leukocytes and neutrophils when exposed to hypoxia ± infectious stimuli. We isolated these cells before and after the expedition, to see if a prolonged period of exposure to hypoxia during the expedition leads to a silencing of gene expression that is maintained in new populations of these cells. We are investigating whether this influences the responses of these cells to hypoxia and infection.

The specific objectives of the primary research question were:

- To characterise leukocyte and neutrophil gene expression when cultured in hypoxia ± infectious stimuli before exposure to systemic hypoxia
- To characterise leukocyte and neutrophil gene expression in response to prolonged systemic hypoxia on the expedition
- To characterise leukocyte and neutrophil gene expression when cultured in hypoxia ± infectious stimuli after exposure to systemic hypoxia
- To compare leukocyte and neutrophil gene expression data taken from before and after exposure to systemic hypoxia
- To examine changes to the processes which control gene expression (e.g. DNA methylation) and protein expression which occur concurrently with these changes in gene expression

In addition to the primary question, there were several secondary research objectives in this study exploring the effect of hypoxia on human physiology and the interplay between personality and altitude symptomatology:

#### *i.* The effect of hypoxia on neutrophil apoptosis:

- To characterise neutrophil apoptosis when cultured in hypoxia ± infectious stimuli before and after exposure to systemic hypoxia
- To compare neutrophil apoptosis data taken from before and after exposure to systemic hypoxia

#### *ii. The effects of hypoxia on platelet reactivity:*

- To confirm that hypoxia-induced platelet hyper-reactivity is ADP-specific
- To determine whether the P2Y1 or P2Y12 pathway mediates hypoxia-induced sensitivity to ADP

• To determine if P2Y12 inhibition is efficacious despite hypoxia-induced platelet hyper-reactivity to ADP

#### *iii. The effects of hypoxia on global macular function:*

- To perform a handheld App test of global macular function, at low- and high-altitude
- To compare and contrast the global macular function with visual acuity
- To determine whether macular function is impaired at high-altitude, and the degree of this impairment
- To evaluate macular adaptation to altitude

#### iv. The effects of hypoxia on saccadic eye movements (an objective measure of cognitive function):

- To test saccadic eye movements, via prosaccade and antisaccade tasks at low- and high-altitude
- To quantify the percentage of direction errors, the time to onset of the eye movement (saccadic reaction time), and the metrics and dynamics of each movement (amplitude, peak velocity, duration)
- To determine whether saccadic eye movements are impaired at high-altitude, the degree of this impairment, and whether eye movements improve during acclimatisation

#### v. The effects of hypoxia on the eye's fundus:

- To evaluate fundus images for retinal whitening, cotton wool spots, new features of high-altitude retinopathy, and changes to retinal vasculature
- To explore whether the genes active in APEX 4's volunteers who had evidence of fluid on the lung are active in APEX 5 volunteers who have fluid at the back of their eye (shown by retinal whitening)

#### vi. The effect of hypoxia on frataxin expression in peripheral blood mononuclear cells:

- To determine the presence/absence of an abnormal version of the frataxin gene (which, when present in pairs, causes Friedreich's ataxia) by genetic analysis
- To investigate frataxin expression after exposure to systemic hypoxia

#### vii. The influence of expression quantitative trait loci on gene expression in hypoxia:

• To determine the effect of differential eQTLs in humans on gene expression when exposed to a prolonged period of hypoxia

#### viii. The effect of personality trait on perceived severity of altitude sickness

- To determine how an individual's personality, and their associated personality traits, alter how that individual perceives the symptoms of altitude sickness (looking at altitude sickness as a whole, and also two specific symptoms: headache and sleep disturbance)
- To compare the symptoms that an individual experiences at high altitude with those of an individual at low altitude

## Expedition dates and research itinerary

**Expedition dates:** 19<sup>th</sup> to 30<sup>th</sup> June 2017

A summary of the research activity each day can be found in the table below:

Day	Location	Study
Baseline testing (pre- expedition)	Edinburgh	All – Eye studies, questionnaires, Neo Five Factor Personality inventory Up to 65ml of venous blood taken for analysis of leukocyte gene expression (including DNA methylation and protein expression), neutrophil apoptosis, platelet reactivity, full blood count, genomic DNA (eQTLs), and frataxin gene expression
1	La Paz	All – Questionnaires of altitude illness
2	La Paz	All – Questionnaires of altitude illness
3	La Paz	All – Questionnaires of altitude illness
4	La Paz	All – Questionnaires of altitude illness
5	La Paz / Huayna Potosí	All – Questionnaires of altitude illness
6	Huayna Potosí	All – Eye studies, questionnaires of altitude illness Up to 60ml of venous blood taken for analysis of leukocyte gene expression (including DNA methylation and protein expression), neutrophil apoptosis, platelet reactivity, full blood count and frataxin gene expression
7	Huayna Potosí	All – Questionnaires of altitude illness
8	Huayna Potosí	All – Eye studies, questionnaires of altitude illness
9	Huayna Potosí	All – Questionnaires of altitude illness
10	Huayna Potosí	All – Eye studies, questionnaires of altitude illness
11	Huayna Potosí	All – Questionnaires of altitude illness Up to 60ml of venous blood taken for analysis of leukocyte gene expression (including DNA methylation and protein expression), neutrophil apoptosis, platelet reactivity, full blood count and frataxin gene expression
12	Huayna Potosí / La Paz	All – Questionnaires of altitude illness
Post- expedition	Edinburgh	Up to 60ml of venous blood taken for analysis of leukocyte gene expression (including DNA methylation and protein expression) and neutrophil apoptosis

### **Next steps**

We are currently analysing our research data and aim to present at national and international conferences and publish our results in due course. We have submitted an abstract from our neutrophil research to the "Therapeutic Targeting of Hypoxia-Sensitive Pathways" Keystone Symposium, an international hypoxia meeting, to be held in Oxford in April 2018.

We also aim to publish and present on the subject of organising a medical research expedition as students, and the benefits this has brought to both the expedition organising team and to our student volunteers. We presented on this theme to the University of Edinburgh Medical Education Forum in September 2017 and at the World Extreme Medicine Expo, in Edinburgh, in November 2017. We have also submitted a proposal to present at the inaugural Learning and Teaching Conference at the University of Edinburgh in June 2018.

We also aim to produce an expedition photo book regarding our experiences.

#### Suggestions for future research

Future research depends on the results of our research projects.

We established a partnership with the haematology laboratory group at SELADIS, in La Paz. SELADIS assisted with basic blood analysis, freezer space, clinical waste disposal, and sourcing laboratory equipment. We hope to collaborate on research projects in the future, as they are also keen to investigate the impact of low oxygen on the haematological system (with regards to blood clotting).

#### APEX 6

We hope that members of the APEX 5 expedition team will be inspired to undertake their own high altitude research expedition, APEX 6. We will offer support and guidance to the next organising committee.

## Conclusion

APEX 5 was a great success, and we achieved all of our research and expedition aims, collecting all data despite the significant challenges we faced. The organising committee and the expedition team as a whole adapted well to the change of location to make this happen.

Data analysis and interpretation is on going, and we are excited by our preliminary findings.

We aim to publish and present our research results in due course and will update our social media accounts and website when this happens.

## Acknowledgements

This report has been guided by the Royal Geographical Society's "*Guide To Writing Expedition Reports*", with thanks also to APEX 4's Expedition Report (authored by Calum Stannett) for inspiration.

We would like to thank the following organisations and individuals for their generous support of the APEX 5 Expedition:

Alpkit	Ober Consulting
Apex Charity	Peek Vision
BMG LABTECH	Philip Harris
Edinburgh Fund	Professor Minns
Edinburgh Medical School	QInstruments
Epipole	SciQuip
Genlab Ltd.	STEMCELL Technologies
Hettich Lab Technology	The Principal of the University of Edinburgh
Medic One	Tiso
myVisionTrack	Tunnock's
Nairn's Oatcakes	Vital Art and Science, LLC

We are very grateful for research grants from the following bodies:

Alpkit Foundation
Captain Scott Society (Spirit of Adventure Award)
Gilchrist Educational Trust
Innovation Initiative Grants, The University of Edinburgh
Mount Everest Foundation
Scottish Mountaineering Trust
The Carnegie Trust for the Universities of Scotland (Vacation Scholarship)
Waddilove Foundation
Wilderness Medical Society (Charles S Houston Grant)

We would like to thank the staff of the Queen's Medical Research Institute, Edinburgh for allowing us to use their facilities free of charge, and for all of their assistance.

We would also like to thank the SELADIS haematology laboratory team for their help with clinical waste and sharps disposal, freezer storage, and full blood count analysis of our samples. We look forward to collaborating in the future.

We are very grateful to Dr Fanney Kristmundsdottir and Professor Moira Whyte of Edinburgh Medical School for believing in us and for all of their support.

We are very grateful to all of our research supervisors, including Dr Ian MacCormick, Dr Paul Knox, Professor Sarah Walmsley, and Dr Alexander Weiss.

We are very grateful for the support of our collaborators at Barts and The London School of Medicine and Dentistry, and would specifically like to thank Dr Melissa Chan who invested considerable time in the platelet research.

We are very grateful to the APEX 4 organising committee, particularly Shona Main, the Expedition Leader, for all of their support and advice.

We would also like to thank: Anne Grant; Steven McLean; Carolynn Walthew; Geraldine Halliday; Simon Beames (and the University of Edinburgh's Expedition Committee); Chris Coner; Sandra Wyllie; Ranald Leask; Ronald Kerr; Gerry Crabbe; Matt Wilkes; Lizett Foronda; Kristina Benova; Marco Soria.

Above all, we would like to acknowledge Dr Kenneth Baillie and Dr Roger Thompson, whose support has been unwavering and invaluable.

Thank you all so much.