

## **START UP RESEARCH FUNDS - INDEPENDENT RESEARCH**

1. The **REQUEST FOR FUNDING FOR RESEARCH PROJECT** must be completed and signed by the investigator and their supervisor.
2. An **ABSTRACT** of the proposal (**maximum of 300 words**).

We conducted the Pan African Pulmonary Hypertension Cohort study (PAPUCO), a prospective observational cohort study of all case of PH has been conducted in 9 centres across 4 African countries, namely Cameroon, Mozambique, Nigeria and South Africa. In all centres, the primary investigator (PI) was a clinician cardiologist experienced in diagnosis of pulmonary hypertension (PH) using echocardiography. The main analysis showed that among the 209 adults included (median age 48years), most of whom had advanced disease; 66% were in World Health Organization Functional Class III-IV, PH types were dominated by PH due to left heart disease (69% PHLHD). We are seeking for funds to do subgroup analysis with the aim of better understanding characteristics, predictors and clinical outcomes in PHLHD. Publishing these data will help fill some of the gaps on PHLHD in sub Saharan Africa (SSA) and plan future trials.

3. A **CONCEPT EXPLAINED**: single spaced, 12 pt.

✓ **Statement of the Research Problem**

The worldwide epidemiology of pulmonary hypertension (PH) as a whole is still to be fully characterised. It is estimated that almost 98% of the global PH burden occurs in low income countries with a population of up to 64 million people at risk but who are undiagnosed (1). PH due to left heart disease has been credited to be the most frequent type of PH (1), but we are not aware of any report on clinical predictors and outcome of PHLHD in Africa and data is scanty at best.

✓ **Brief Literature Review (with references)**

The main analysis of the PAPUCO registry (2) highlighted the importance of PH-LHD as the predominant type of PH. PHLHD frequently occurs as a manifestation of left heart systolic or diastolic dysfunction, but also to a lesser extend valvular disease. The existing reports have almost exclusively focused on selected groups of Caucasian patients with heart failure (HF), few using right heart catheterization, but the majority using non-invasive assessment of the right ventricular systolic pressure (RVSP) with echocardiography. Several studies of HF have reported that, compared with western countries, HF in sub Saharan Africa (SSA) populations occurs two decades earlier and is predominantly of non-ischemic origin, including some conditions that are now exceptional in western countries, but still has a poor prognosis (3). How this particular phenotype of HF affects the landscape of PHLHD and conversely how PHLHD could influence

HF prognosis in our region is still unknown, yet this information is needed to assist the stratification of patients with PH-LHD risk in daily clinical practice.

In this study, we will investigate the determinants of pulmonary pressure, clinical and echocardiographic profile, outcome and their predictors in the specific population of patients with PH-LHD using the PAPUCO registry.

### References:

1. Dzudie A, Kengne AP, Thienemann F, Sliwa K. Predictors of hospitalisations for heart failure and mortality in patients with pulmonary hypertension associated with left heart disease: a systematic review. *BMJ Open*. 2014 Jul 10;4(7):e004843. doi: 10.1136/bmjopen-2014-004843..
2. Thienemann F, Dzudie A, Mocumbi AO, Blauwet L, Sani MU, Karaye KM, Ogah OS, Mbanze I, Mbakwem A, Udo P, Tibazarwa K, Damasceno A, Keates AK, Stewart S, Sliwa K. The causes, treatment, and outcome of pulmonary hypertension in Africa: Insights from the Pan African Pulmonary Hypertension Cohort (PAPUCO) Registry. *Int J Cardiol*. 2016 Jun 29;221:205-211.
3. Damasceno A, Mayosi BM, Sani M, Ogah OS, Mondo C, Ojji D, Dzudie A, Kouam CK, Suliman A, Schrueder N, Yonga G, Ba SA, Maru F, Alemayehu B, Edwards C, Davison BA, Cotter G, Sliwa K. The causes, treatment, and outcome of acute heart failure in 1006 Africans from 9 countries. *Arch Intern Med*. 2012 Oct 8;172(18):1386-94.

### ✓ Objectives of the Study

#### ○ Aims

To investigate the determinants of pulmonary pressure, clinical and echocardiographic profile, outcome and their predictors in the specific population of patients with PH-LHD using the PAPUCO registry.

○ **Design:** Prospective multicenter cohort registry

#### ○ Specific hypotheses

We hypothesize that the determinants of pulmonary pressure, the clinical and echocardiographic profile, outcome and their predictors in of patients with PLHD in SSA will be different from what has been observed in Caucasians.

### ✓ Method of Investigation (what will you do and how will you do it)

○ **Experimental rationale:** Not applicable

○ **Procedure/Methodology:** We have measure right ventricular systolic pressure as indicated in the the previously published PAPUCO method (4)

Ref 4: Thienemann F, Dzudie A, Mocumbi AO, Blauwet L, Sani MU, Karaye KM, Ogah OS, Mbanze I, Mbakwem A, Udo P, Tibazarwa K, Ibrahim AS, Burton R, Damasceno A, Stewart S, Sliwa K. Rationale and design of the Pan African Pulmonary hypertension Cohort (PAPUCO) study: implementing a contemporary registry on pulmonary hypertension in Africa. *BMJ Open*. 2014 Oct 14;4(10):e005950. doi:10.1136/bmjopen-2014-005950.

○ **Data Analysis**

Data will be processed and analysed using the SPSS software version 20.0 for Windows. Patients with mild to moderate will be arbitrarily categorized according to RVSP level as: mild if RVSP was 36-50 mmHg and moderate if RVSP was 51-60 mmHg. Categorical variables will be presented as frequencies and percentages, while continuous variables will be presented as means and standard deviation (SD), or median (25<sup>th</sup> to 75<sup>th</sup> percentiles). Comparison between groups will use appropriate parametric and non-parametric tests. Linear regressions will be used to identify the independent predictors of RVSP. Kaplan Meier estimators will be employed to depict the outcome (mortality or admissions) over time across major subgroups and differences assessed with the log rank test. Cox regressions will be used to investigate determinants of admissions between the three PH groups during follow up. A p-value <0.05 will be considered statistically significant.

✓ **Significance of this research.**

This study will fill several gaps in the knowledge about PHLHD and suggest future research questions.

✓ **Outcome from seed funding and how this will advance your research**

The main outcome from this funding will be the publication of our paper on PHLHD. The publication will consolidate our network of investigators of PHLHD and motivate us towards initiation of a second phase (PAPUCO II). PAPUCO II will aim at understanding the mechanisms of the disease but also test the relevance of PH as a therapeutic target in clinical randomized trial.

**4. A BUDGET.**

| Items   | Costs (USD) | Justification   |
|---|-------------|---|
| Update of the software to SPSS version 24             | -           | Software is available   |
| Conception of sample spreadsheet                      | 600         | We need a new data entry by a second operator and verification for accuracy |
| Data entry  | 1000        |   |
| Verification of data entry                            | 400         |   |
| Analyzing categorical and numerical Data              | 1000        |   |
| Interpretation, drafting of summary and making curves | 700         |   |
| Writing of the publication                            | 1300        |   |
| Total   | 5000 USD    |   |

5. A Brief bio sketch of applicant (one page)

The applicant (Anastase) is a senior consultant cardiologist and head of cardiac intensive care unit and pacing at the Douala General Hospital, and lecturer of clinical medicine at Buea Faculty of Health Sciences and university of Yaounde 1, Cameroon. Anastase received training in all aspects of clinical cardiology and in clinical research. After his general training in 1998 and having worked as a general physician for two years, did a certified training as an internal medicine physician in Cameroon. I then further trained in general cardiology, with certified training in cardiac echography and cardiac pacing at Louis Pradel's cardiovascular hospital and Claude Bernard University Lyon, France. My training in clinical research paralleled my training in clinical medicine and I earned my PhD at the University of Cape Town, South Africa. I have published more than 60 papers in clinical medicine and co authors 03 chapters of the book entitled "Heart of Africa". Substantial leadership in clinical research has been gained since I co founded and now chair the Clinical Research Education, Networking and Consultancy (CRENC), an organization of independent investigators, research consultants and clinicians with dedicated time to research. I have previously participated as country PI in a number of multicentric and multinational studies in the field of clinical cardiovascular medicine including THESUS-HF, RELY AF, PAPUCO I, BAHEF clinical trial. Our current area of expertise and current research focus is systemic hypertension, heart failure, pulmonary hypertension due to left heart disease and arrhythmias.

**Applicant:**

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Signature



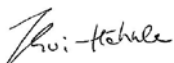
Date: 12 october 2016

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Signature

Prof Karen Sliwa

Date: 15 October 2015.