

**PROCORE - FRANCE/HONG KONG JOINT RESEARCH SCHEME
COMPLETION REPORT**

Project Reference Number

F-HK13/10T

Project Title

Orphan nuclear receptors, estrogen-related receptors (ERRs), as new targets in hormone-dependent prostate and breast cancers

Particulars

	Hong Kong team				French team			
Name of Project Co-ordinator (with title)	English: CHAN Leung Franky, PhD Chinese: 陳良				Jean-Marc VANACKER, PhD			
Name of Co-Investigator (if any)	English: ZOU Chang Chinese: 邹暢							
Institution or Institutional affiliation	<input type="checkbox"/>	CityU	<input type="checkbox"/>	HKU	<input type="checkbox"/>	CEA	<input type="checkbox"/>	INRA
	<input checked="" type="checkbox"/>	CUHK	<input type="checkbox"/>	HKUST	<input checked="" type="checkbox"/>	CNRS No.	<input type="checkbox"/>	INRIA
	<input type="checkbox"/>	HKBU	<input type="checkbox"/>	LU	<input type="checkbox"/>	INFREMER	<input type="checkbox"/>	INSERM No.
	<input type="checkbox"/>	HKIED	<input type="checkbox"/>	PolyU	<input checked="" type="checkbox"/>	University of	Lyon	
					<input checked="" type="checkbox"/>	Others: Ecole Normale Supérieure de Lyon		
Other project team members (if any)								

Funding Period

	1 st year	2 nd year (if applicable)
Start Date	1/1/2011	
Completion Date	31/12/2011	

Objective(s) as per original application

1. To determine the roles of ERRs in prostate and breast cancer cell migration and invasion
2. To determine the significance of ERRs in androgen-signaling in hormone refractory prostate cancer
3. To evaluate the significance of ERR α in infiltration of immune cells in inflamed prostatic stroma
4. To determine the significance of functional silencing of ERR α on in vivo growth of prostate cancer

[Please attach relevant document(s)]

i) Outline of proposed research and results obtained

In this proposed study, we planned to study the functional significance of members of orphan nuclear receptors estrogen-related receptors (ERRs) in two hormone-dependent cancers, prostate and breast using different in vitro and in vivo models established in both PIs' laboratories. Our preliminary results obtained so far are summarized as follows:

- 1) ERR α could function to promote breast cancer cell migration capacity via its negative regulation on the turnover of a GTPase RhoA.
- 2) ERR α could interfere androgenic/AR signaling in prostate cancer cells via its interaction with a histone demethylase LSD1 and epigenetic regulation.
- 3) Overexpression of ERR α could induce in vitro growth resistance to androgen-ablation condition (charcoal-stripped serum) and anti-androgen (bicalutamide) in prostate cancer cells likely via both AR-dependent (suppression of AR mRNA levels) and undefined AR-independent mechanisms.

ii) Significance of research results

Our results showing for the first time that orphan nuclear receptor ERR α could contribute to the advanced growth of breast and prostate cancers via its functional regulation on breast cancer cell migration via a RhoA-dependent mechanism and also hypoxic growth adaptation of prostate cancer cells in a HIF-1-dependent manner; and also suggest a potential value of ERR α as a therapeutic target for treatment of advanced prostate and breast cancers.

iii) Research output

Based on the results obtained by both teams (partially supported by this PROCORE-France/HK Joint Research Scheme), one manuscript on the role of ERR α on breast cancer cell migration has been submitted for publication by the French PI, while another manuscript on the functional study of ERR α on hypoxic growth regulation of prostate cancer cells is being prepared for submission by the HK PI. Both manuscripts are in collaboration, *i.e.* both PIs are co-authors of the papers.

iv) Potential for or impact on further research collaboration

Based on the encouraging preliminary results obtained by two collaborating teams in this proposed study in past two years, the HK and French PIs have recently submitted a joint grant application to the French National Research Agency (ANR)-Hong Kong RGC Joint Research Scheme 2013-2014 to support a 3-year collaborative study on ERR α in hormone-dependent and -independent prostate and breast cancers. It is also happy to learn that this joint grant application has been recently shortlisted by CUHK for its submission to RGC for further review.