Research program on ZIKV infection in pregnant women and their offspring in French West Indies and French Guyana French Territories in America, FTA
DFA: FWI and FG, an outlook

Guadeloupe
Pop: 400,000

Martinique
Pop: 380,000

French Guiana
Pop: 255,000
Pre-existing network structure and network capacity

- Centre d'investigation clinique (Inserm CIC 1424)
  - One CIC with 3 sites, one in each territory
  - Sponsored by Inserm
  - Emerging infectious diseases and genetic diseases in tropical areas
  - Observational and interventional clinical research

- Caribbean Arovirosis cohort (CARBO)

- REACTing
  - Prior experience with the Chikungunya outbreak in 2014
  - Preparation of clinical research as early as December 2015, case of ZIKV infection was identified in the FTA
Clinical studies and clinical trials

• **Observational**
  – CARBO
    • Neuro-CARBO
    • ARBHITA
    • ZIKASMELL
  – ZIKA-DFA-FE

• **Interventional**
  – ZIKA-DFA-BB
  – Vaccine trial
    • VRC 704: Phase 2 RCT on CHIKV vaccine (ongoing)
    • VRC 705: Phase 2/3 RCT on ZIKV vaccine (planned)
Efforts to develop rapid clinical response to EID

**ZIKA-DFA-FE**
- Jan 4: project writing starts
- Feb 5: regulatory frame for research defined (noninterventional research, sponsor Inserm)
  - Authorizations to be obtained from national IRB, CCTIRS (Advisory committee on personal information management in the field of health research), and CNIL (Committee for information technology and freedom)
- Feb 16: all application files completed and dispatched, along with a request by the Director General of Health (MoH) to expedite evaluation
- Mar 4: all authorizations granted

**ZIKA-DFA-BB**
- Feb 29: project writing starts
- April 10: regulatory frame for research defined (biomedical research, sponsor Inserm)
  - Authorizations to be obtained from national IRB and ANSM (French Medicines Agency)
- April 20: all application files completed and dispatched
- May 6: all authorizations granted
Collaboration with other networks

• Clinical research strongly and effectively linked to
  – Care (hospitals of the 3 FTAs)
  – epidemiological surveillance (CIRE Antilles-Guyane, regional agency of the French National Public Health Agency)

• Committed and open to collaborative research
  – ZIKALLIANCE
  – Other research teams
    • IRSET: identification of environmental cofactors (ZIP study)
    • ...

• Open to data sharing
Epidemiological situation of Zika in the FTA, Nov 2016

Martinique

Guadeloupe

Guyane

St Martin

St Barth
Objectives of the ZIKA-DFA studies (1)

- ZIKA-DFA-FE
  - Measure the incidence of ZIKV infection during pregnancy
  - Describe clinical manifestations of the disease during pregnancy
  - Measure the incidence of microcephaly diagnosed in utero and at birth
  - Identify other complications not yet identified as possible complications of ZIKV
  - Measure relative risk of birth defects /other complications, with a focus on the role of
    - Gestational age at the time of ZIKV infection
    - Symptomatic ZIKV infection
Objectives of the ZIKA-DFA studies (2)

- **ZIKA-DFA-BB**
  - Describe abnormalities in and follow-up of apparently healthy children born to mothers infected with ZIKV during pregnancy (Cohort 1)
  - Follow-up children born with defects to mothers infected with ZIKV during pregnancy (Cohort 2)
  - Quantify the risks of complications in fetuses/children born to mothers infected with ZIKV, weighted by gestational age at the time of infection and exposure to cofactors. For this purpose, a cohort of healthy children born to uninfected mothers will be assembled (Cohort 3)
ZIKA – DFA – FE : 5 work packages

• **WP1**: identification and follow-up of pregnant women presenting with clinical symptoms of acute ZIKV infection, at any time of pregnancy
• **WP2**: follow-up of pregnant women in whom embryofetopathy is suspected during pregnancy ultrasound monitoring
• **WP3**: build up a serum collection from blood samples drawn once per trimester in any pregnant woman throughout the Zika outbreak
• **WP4**: build up a collection of mother and cord blood sampled the day of delivery in any delivering woman throughout the Zika outbreak
• **WP5**: build up a collection of maternal blood and fetal tissues in women in whom pregnancy, started during the Zika outbreak, would terminate with abortion, fetal death, or medical pregnancy termination
Observational studies of the consequences of ZIKV infection in the course of pregnancy during the 2016 outbreak of Zika in the FTA (ZIKA-DFA-FE)

WP1
Clinical symptoms of acute ZIKV infection
Blood and urine RT-PCR within 10 days of 1st symptoms
ZIKV Serology
Prenatal monitoring: monthly fetal ultrasound until delivery
If abortion, fetal death, or medical termination of pregnancy, see WP5

WP2
Suspected embryofetopathy during ultrasound monitoring of pregnancy
ZIKV serology (neutralization)
Prenatal monitoring: monthly fetal ultrasound until delivery, ± amniocentesis ± MRI at W30-34
If abortion, fetal death, or medical termination of pregnancy, see WP5

WP3
Serum collection from blood samples drawn once per trimester in any pregnant woman
ZIKV serology q trimester
Fetal ultrasound at GW12, GW22, GW28, GW32, GW36

WP4
Collection of mother and cord blood sampled the day of delivery
ZIKV serology in mother + blood cord biobank
In case of stillbirth, see WP5

WP5
Collection of maternal blood and fetal tissues if abortion, fetal death, or medical pregnancy termination
ZIKV serology (neutralization)
Fetal autopsy, fetal tissue storage
Placenta: ZIKC RT-PCR ZIKV & histopathology
If abortion, fetal death, or medical termination of pregnancy, see WP5
Observational studies of the consequences of ZIKV infection in the course of pregnancy during the 2016 outbreak of Zika in the FTA (ZIKA-DFA-FE).

If abortion, fetal death, or medical termination of pregnancy, see WP5.

Clinical symptoms of acute ZIKV infection
Blood and urine RT-PCR within 10 days of 1st symptoms
ZIKV Serology
Prenatal monitoring: monthly fetal ultrasound until delivery

WP1
N=1,800

Suspected embryofetopathy during ultrasound monitoring of pregnancy
ZIKV serology (neutralization)
Prenatal monitoring: monthly fetal ultrasound ± amniocentesis & MRI at W30-34

WP2
N=120

Serum collection from blood samples drawn once per trimester in any pregnant woman
ZIKV serology q trimester
Fetal ultrasound at W12, W22, W28, W32, W36

WP3
N=10,000

Collection of mother and cord blood sampled the day of delivery
ZIKV serology & blood biobanking

WP4
N=9,000

Collection of maternal blood and fetal tissues if abortion, fetal death, or medical pregnancy termination
ZIKV serology (neutralization)
Fetal ultrasound, amniocentesis, & MRI
Placenta: ZIKV & histopathology

WP5
N=60

In case of stillbirth, see WP5.

Expected numbers (3 FTA) over a 1-year period

N=10,000
N=1,800
N=9,000
N=120
N=60
N=1,800
N=1,800
Observational studies of the consequences of ZIKV infection in the course of pregnancy during the 2016 outbreak of Zika in the FTA (ZIKA-DFA-FE).

If abortion, fetal death, or medical termination of pregnancy, see WP5.

Clinical symptoms of acute ZIKV infection:
- Blood and urine RT-PCR within 10 days of 1st symptoms.
- ZIKV Serology.

Prenatal monitoring:
- Monthly fetal ultrasound until delivery.

WP1
- N=2576 (3 FTA), by Nov 7, 2016.
- N=118 Mar 27 Guy 89 Gua 2
- N=106 Mar 25 Guy 68 Gua 13
- N=907 + 590 Gua 235

WP2
- Suspected embryofetopathy during ultrasound monitoring of pregnancy: ZIKV serology.
- Prenatal monitoring: monthly fetal ultrasound ± amniocentesis ± MRI at W30-34.

WP3
- Serum collection from blood samples drawn once per trimester in any pregnant woman.
- ZIKV serology q trimester.

WP4
- Collection of mother and cord blood sampled the day of delivery.
- ZIKV serology in mother + blood cord biobanking.
- ZIKV serology in mother + blood cord biobanking.

WP5
- Collection of maternal blood and fetal tissues if abortion, fetal death, or medical termination of pregnancy.
- ZIKV serology.
- Fetal autopsy, fetal tissue storage.
- Placenta: ZIKV RT-PCR ZIKV & histopathology.
- In case of stillbirth, see WP5.
AGNOWLEDGMENTS

• 3 FTA
  – Clinical Investigation center (CIC) of Antilles-Guyane
  – Gynecologists-obstetricians and pediatricians
  – Biological Resource Centers (CRB) of Guadeloupe and Martinique

• Pôle recherche clinique INSERM

• Unité d'épidémiologie des maladies émergentes, Institut Pasteur

• REACTing