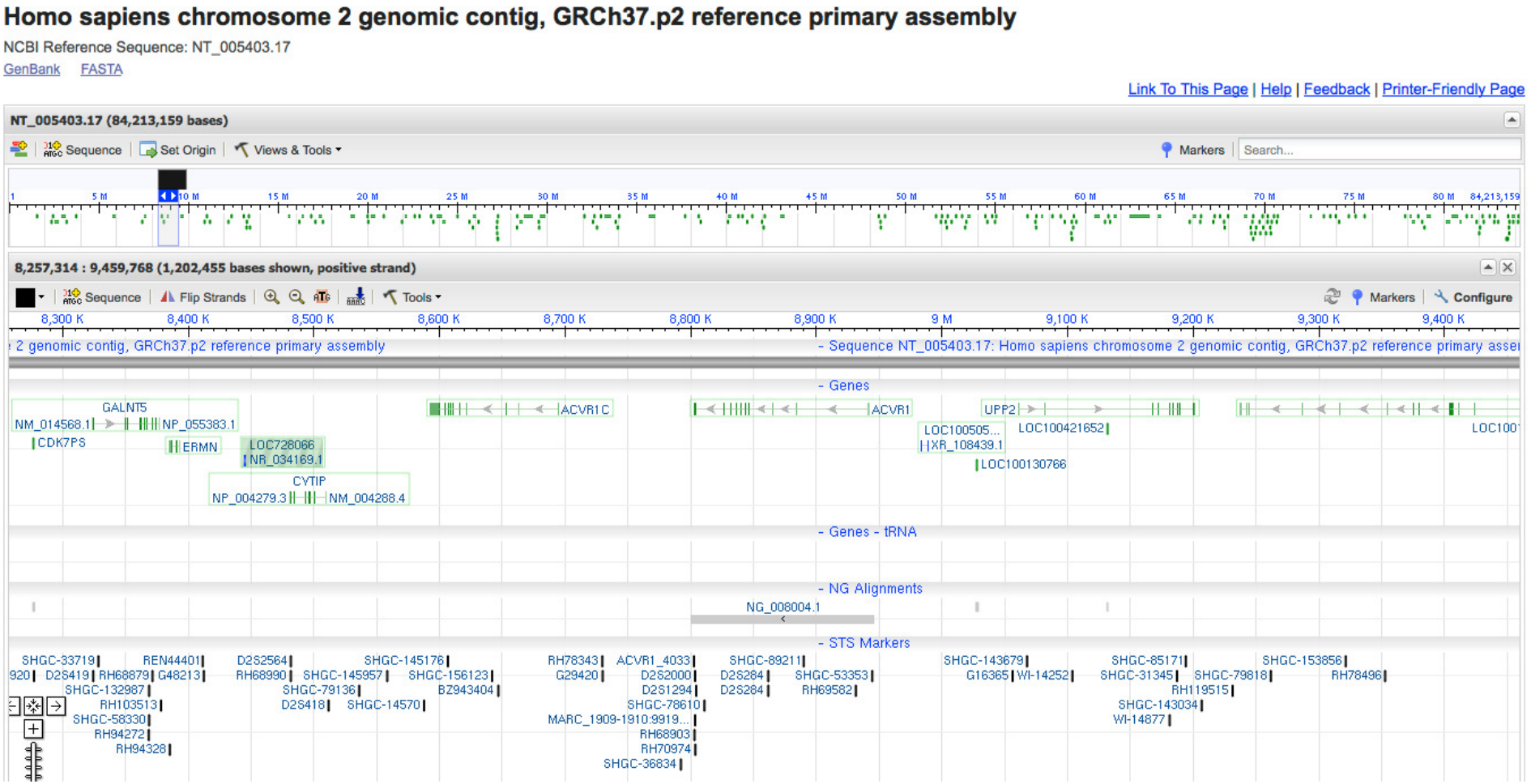
Re-sequencing the ACVR1 genomic region in patients



WHY ?

- It might be interesting to relate sequence variants with phenotypic features

- It might be interesting to find variants potentially involved in gene regulation

Which part of the genomic region ?

All the region including the ACVR1 gene plus the two flanking genes (UPP2 and ACVR1C) on both sides

How many samples ?

As many patients as possible

Controls

Induced Pluripotent stem cells (iPSC)

Generating iPSCs from patients. When a patient has to udergo some surgical intervention it might be worthy to take a sample of skin to grow fibroblast cells that can be treated to obtain iPS

WHY ?

iPSCs are non-transformed cells that can undergo different types of differentiation, then represent a good cellular model to study disease mechanism

Other attempts to obtain multipotent progenitors from patients proved to be difficult, such as obtaining cells from decidual teeth

An objective of the international FOP community could be to build up a bank of iPSCs from FOP patients

What is needed?

A group expert in the technology (or money to pay companies that produce cells commercially)

Drug discovery for FOP treatment options

Different strategies can be used to this aim

Different groups are approaching this issue

Should a coordination / updating forum be useful for the international FOP community?

An expected European call for research funding, that includes research on rare diseases

Working paper

for 2012

research funding for the Health theme

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2.4.4 Rare diseases

The focus will be on EU-wide studies of natural history, pathophysiology and on development of preventive, diagnostic and therapeutic interventions, including rare Mendelian phenotypes of common diseases. This area should help identifying and mobilising the critical mass of expertise in order (i) to shed light on the course and/or mechanisms of rare diseases, or (ii) to test diagnostic, preventive and/or therapeutic approaches, to alleviate the negative impact of the disease on the quality of life of the patients and their families, as appropriate depending on the level of knowledge concerning the specific (group of) disease(s) under study.

For this call for proposals the topics will focus on the preclinical and clinical development of orphan drugs, and on the conduction of observational trials for those rare diseases treated off-label, aiming to improve clinical practices in the management of these diseases. These efforts will be complemented with coordination action activities aimed at identifying and exchanging best practices in the clinical management of rare diseases.

Note: Depending on the topics listed below, applicants will have to follow the rules for **two-stage or single-stage submission procedure (see also respective call fiche in section III).**

HEALTH.2012.2.4.4-1: Preclinical and/or clinical development of substances with a clear potential as orphan drugs. Support will be provided to preclinical studies (pharmacological, pharmacodynamics, pharmacokinetics and toxicological) in models and/or clinical studies (including phase III clinical trials) of EU designated orphan medicinal products. Clinical studies should focus on biopharmaceutical studies (including bioavailability, bioequivalence, *in vitro-in vivo* correlation), human pharmacokinetic and pharmacodynamic studies, human efficacy and safety studies. Clinical trials must be appropriately powered to produce statistically significant

evidence. Involvement of industry, in particular SMEs, is strongly recommended. Diagnostics and therapies for cancer and nervous system diseases will not be considered. The orphan medicinal product will need to be granted the EU orphan designation at the latest on the date of the call closure[22]. It is expected that the project will have appropriate plans to engage with relevant stakeholders such as patient organisations and the European Medicines Agency. **Note:** Limits on the EU financial contribution apply. These are implemented strictly as formal eligibility criteria.

Funding scheme: Collaborative Project (medium-scale focussed research project)

Requested EU contribution per project: Maximum EUR 6 000 000

One or more proposals can be selected.

Expected impact: The project(s) should deliver appropriate information to i) start clinical development of orphan drugs (if the project includes preclinical development) and/or ii) improve care of rare diseases patients (if the project includes clinical development). Collected data should be of sufficient quality to be further exploited in marketing authorisation requests.

Additional eligibility criterion: Projects will only be selected for funding on the condition that the estimated EU contribution going to *industry is 30%* or more of the total estimated EU contribution for the project as a whole. This will be assessed at the end of the negotiation, before signature of the grant agreement. Proposals not fulfilling this criterion will not be funded.

Justification: *This topic is of interest to DG SANCO. 10 years after the EU orphan drug regulation, 62 orphan medicines have been approved for use in the EU, giving treatment options for 53 different rare diseases. 720 orphan designations were granted (success rate of 65 %). This means that a lot of designated products do not make it to the market, and there is a need to support the clinical development of the designated OD (repeated message from COMP/EMA). The clinical development topic of 4th call has clearly stimulated new applications for OD designation (as mentioned by COMP chair and EMA staff). An important fraction of sponsors for orphan-designated products are SMEs which need incentives to bridge the gap from designation to clinical studies. In addition, orphan drugs being often based on innovative technologies, this would contribute to boost innovation in Europe. Such a topic could offer a link with US initiatives (NIH), and could also attract SME participants.*

HEALTH.2012.2.4.4-2: Observational trials in rare diseases. The aim is to improve clinical practice in the management of rare diseases patients, and research should include the comparison of outcome of various prevention or treatment/intervention regimens for those rare diseases for which no orphan drug is available and that are being treated off-label. Studies should include the evaluation of effectiveness and adverse events. Particular attention should be given to the definition of appropriate outcome measures. Therapies for cancer, infectious diseases and nervous system diseases will not be considered. Project should include appropriate plans to engage with relevant stakeholders such as patient organisations and dissemination plans to ensure the wide and rapid uptake of developed guidelines. Child health aspects should be taken into consideration whenever appropriate. **Note:** Limits on the EU financial contribution apply. These are implemented strictly as formal eligibility criteria.

[22] The European register of designated Orphan Medicinal Products is available from http://ec.europa.eu/health/documents/community-register/html/alforphreg.htm

Funding scheme: Collaborative Project (small-scale focussed research project)

Requested EU contribution per project: Maximum EUR 3 000 000

One or more proposals can be selected.

Expected impact: The project(s) should lead to accepted evidence-based clinical guidelines for a better care of patients afflicted by rare disease(s) for which no dedicated treatment is currently available.

***Justification**: This topic is of interest to DG SANCO. It is estimated that up to 90% of drug use for rare diseases is off-label (Science 2010, 327, 273-274). Given that orphan drugs are currently available for a minority of rare diseases only, it is important to collect, analyse and compare treatment data in order to capitalize on existing practice, to benefit patients until orphan drugs are marketed.*

HEALTH.2012.2.4.4-3: Best practice and knowledge sharing in the clinical management of rare diseases. This action is dedicated to the development of a networking platform supporting the collection of standardised and validated data and the exchange of information providing evidence for best clinical management of rare diseases. It should also help identifying additional research needs to further improve clinical practice. The platform should not be restricted to particular (groups of) rare diseases and the platform sustainability after the EU financing period must be established during the project. **Note:** Limits on the EU financial contribution apply. These are implemented strictly as formal eligibility criteria.

Funding scheme: Coordination and Support Action (coordinating action)

Requested EU contribution per project: Maximum EUR 2 000 000

Only up to one proposal can be selected.

Expected impact: A recognised, sustainable networking platform facilitating the exchange of information, identifying and spreading best clinical practice for the management of rare diseases should be delivered.

***Justification:** This topic is of interest to DG SANCO and DG ENTER. Such a coordination action would complement the observational trials projects, and offer an EU platform for dissemination of best practices. It would be of high value for patients in a field that crucially lacks therapeutic options.*

2.4.5 Other chronic diseases

The focus will be on non-lethal diseases and chronic conditions with a high impact on the quality of life at old age such as functional and sensory impairment and chronic inflammatory diseases. It is expected that collaborative research in this area will lead to improved diagnostics of the chronic conditions, develop tools and/or intervention strategies, which may contribute to delaying the onset of chronic diseases, their efficient treatment, and improving quality of life.

Note: For the topics listed below, applicants will have to follow the rules for **two-stage submission procedure (see also respective call fiche in section III).**

Are we interested ?

Should we try to apply?

Is anybody willing to take the coordination?

International Cooperation

The strategy for international cooperation in Theme Health is many fold: tackling global challenges, such as addressing diseases of poverty, including neglected diseases; improving the competitiveness of the European science base and industry through global cooperation; supporting external relations of the EU, noting that health issues, including health research are shared between all countries, rich and poor. Special efforts will be made by programme level collaborations in rare diseases with the US and probably with other European and international partners, and in innovative therapies with Australia. Specific actions in the area of poverty related diseases are foreseen with developing countries and public health in order to contribute to achieving the Millennium Development Goals.

All topics under Theme Health are open for the participation of international partners from third countries. In recognition of the opening of NIH[15] programmes to European researchers, participants established in the *United States of America* are eligible for funding and participation in all topics described in this work programme.