



Have we finally solve the enigma of the small size of Pygmies?

Yves Le Bouc

► To cite this version:

Yves Le Bouc. Have we finally solve the enigma of the small size of Pygmies?. *Annales d'Endocrinologie = Annals of Endocrinology*, 2017, 78 (2), pp.83-87. <10.1016/j.ando.2017.04.022>. <hal-04026602>

HAL Id: hal-04026602

<https://hal.science/hal-04026602v1>

Submitted on 27 Mar 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

Have we finally solve the enigma of the small size of Pygmies?
L'énigme de la petite taille des pygmées enfin résolue?

Yves Le Bouc

Sorbonne Universités, UPMC Univ Paris 06, Inserm, Centre de Recherche St-Antoine
(UMRS 938), AP-HP, Hôpitaux Universitaires Paris Est, Hôpital des Enfants Armand
Trousseau, Explorations Fonctionnelles Endocriniennes, 75012, Paris, France.

Tel: +33 (0) 1 44 73 64 47

Fax: +33 (0) 1 44 73 61 27

courriel : yves.le-bouc@inserm.fr

Les pygmées sont décrits comme étant parmi les humains les plus petits. Cette petite taille est une énigme qui anime depuis longtemps bon nombre de scientifiques. De nombreuses données concernant le phénotype clinique et biologique, génétiques sont connues ainsi que leur mode de vie, leur culture, leur environnement mais l'étiologie de leur petite taille fait toujours débat. S'agit-il notamment d'une adaptation à la forêt tropicale, de l'impact de l'environnement, d'une particularité génétique ou d'un mix de ces différents paramètres. Concernant l'étude de l'axe somatotrope un déficit sérique en IGF 1 a été observé pour lequel un défaut d'efficacité du récepteur de la GH semble être impliqué. Il reste cependant beaucoup d'incertitudes et d'autres analyses hormonales, génétiques et épigénétiques sont nécessaires et doivent être intégrées dans un cadre d'études multidisciplinaires.

Abstract

Pygmies are considered to be among the smallest humans. Their small size is an enigma that has puzzled numerous scientists. Many data have been collected concerning their clinical and biological phenotypes, genetics, lifestyle, culture and environment, but the reasons for their small size remain a matter of debate. Is it an adaptation to life in the tropical forest, an impact of the environment, an usual genetic feature or a mixture of these factors? Studies of the somatotrophic axis have revealed that serum IGF-1 concentrations are low in this population, probably due to an impairment of the GH receptor. However, many uncertainties remain, and further hormonal, genetic and epigenetic studies will be required in the framework of multidisciplinary studies.

Introduction

The name "pygmy" originates from the small body size of this population. The term "pygmaios" was used by Homer (The Iliad, Song III, 1-6). Etymologically, it designates an ancient unit of length, the cubit (about 45 cm, the distance from the elbow to the wrist). In his book "African Pygmies", Cavalli-Sforza raised the problem of how to define Pygmies. His chosen definition is as follows: "It therefore seems reasonable to call Pygmies groups of Africans who live (or lived until a short while ago) as hunter-gatherers in the tropical forest, and have a stature smaller than that of the farming tribes with which they are in contact and have a relation of servitude". This reference to servitude has largely disappeared from

current definitions of pygmies, which are based, more than the use of a stature threshold, on a specialist forest lifestyle (hunting, gathering, medicinal practice), with its own social organization and complex socioeconomic relationships with non-Pygmy neighbors [1-7]. Pygmies are among the smallest humans known, with the exception individuals with growth-related diseases [4], with statures even smaller than those of *Homo erectus* or *Homo neanderthal* [8,9].

About 20 Pygmy populations speaking different languages (e.g. Aka, Baka, Bongo, Kola, Koya, Tumandwa, Batwa, Babenzi, Binga, Twa, and Efe) are found throughout the equatorial forests extending from east to west over Central Africa. The ancestral non-Pygmy and Pygmy populations seem to have diverged 50 to 70 thousand years ago. Two major groups of Pygmies, those of East and West Africa, diverged about 20,000 years ago, and the Western Pygmies have diverged into a number of smaller groups over the last 3000 years. Genetic analyses of the various Pygmy groups have raised questions about whether they have a common origin or whether they acquired their current stature through a convergence effect. In the case of convergence, small size, a useful adaptation to life in the tropical forest, would have emerged independently in the two regions, West and East Africa [6, 10-12].

The key question that divides opinion and has driven many studies and discussions is that of the cause of the small size of Pygmies. Several evolutionary hypotheses have been proposed: is small size an adaptation to the tropical forest and the impact of its environment (heat/humidity, infection/parasite infestations, the effects on mobility of the density of the forest, and access resources), does it reflect a lifestyle choice involving the choice of particular mates, or is it a genetic feature? [3-6, 11-13].

Growth and puberty

Few data for adult size in Pygmies have been published. The Pygmies from the western region, such as the Baka group (Cameroon) have a mean height of 155.6 cm for men (range: 144-167 cm) and 146.5 cm for women (range: 136.7-146.5 cm). These heights are lower than those of the Nzime population (non-Pygmies from Cameroon) : mean height of 168.5 cm for men (range: 155.5-181.5 cm) and 155.8

cm for women (range: 142.2-169.4 cm). The Pygmies from East Africa are shorter than those of West Africa, with the shortest statures recorded for the Efe and MButi populations (ITURI forest in the Democratic Republic of Congo): mean height of 144 cm for men and 137 cm for women. These populations are shorter than the neighboring Lese population (mean height of 162 cm for men and 152 cm for women). However, no longitudinal studies of individual size have been performed and no growth curves for these populations are available. One of the principal problems encountered in these studies is uncertainty about date of birth [14-18].

Data for birth parameters are sparse and insufficient for any inferences to be made about the mechanisms affecting postnatal growth. Only two publications have provided height and weight data, at birth, for Efe Pygmies (compared to the non Pygmy Lese population) and for Ngayu Pygmies from Ituri Forest (compared to the neighboring non Pygmies Bantou) [14, 17]. Mean birth lengths were 44.6 ± 2.1 cm for the Efe Pygmies and 46.4 ± 1.4 cm for the Lese. Mean birth weights were 2.69 ± 0.46 kg for the Efe Pygmies and 3.07 ± 0.43 kg for the Lese. However, it should be noted that the sample size was very small for these studies ($n = 10$ to 15) and no information was provided about gestational age at birth. Similar results were described for Ngayu Pygmies. The growth of the Efe Pygmies was followed between the ages of six months and five years. A marked decrease in growth rate was observed in Efe Pygmies (height measurements of -2.7 SD (6 months) to -4.1 SD (5years)) that was much greater than that in the Lese (-1.76 SD and -2.11 SD, respectively). Head circumference, determined at birth, was found to be similar in Ngayu Pygmies (Ituri forest) and the non-Pygmy Bantu population (mean: 33.4 cm (range: 32-36 cm) for Ngayu Pygmies and 34.1 (range 30-37 cm) for the Bantu) [14].

No data for birth parameters was available for the Pygmies of Western Africa. Central African Pygmy populations displaying genetic admixture with neighboring non-Pygmy populations are taller, consistent with a genetic impact on the stature of the Pygmy population [5].

There is controversy about the growth velocity of Pygmies during puberty. According to the group of Pygmies have similar growth rates to other populations during childhood, but the Pygmies of the Ituri Forest are small because the pubertal growth peak is entirely absent in boys and very blunt in girls [16].

However, this study was performed on a very small sample (9 male subjects, and 10 female subjects with a mixed tanner stage from 2 to 4, six of whom were already menstruating). Importantly, Bailey et al have focused on frequent uncertainties about the age of Pygmies; moreover, Pygmy populations are nomadic, and the rate at which they mature may be different from that of European and American populations [15,17]. Bailey also noted a height under the 3rd percentile for Pygmies from the Ituri forest during the first year of life, with an increasing growth deficit until the age of five years, after which, growth velocity was maintained until after puberty, with an adult height of about -4 to -5 SD. He therefore concluded that a lower growth rate during childhood, rather than puberty, was the principal cause of small adult size in this population.

We recently described the growth pattern, from birth to adulthood (25 years), of Baka African pygmies for whom birth dates were known with certainty [19]. Body weight at birth within the Baka group is within the normal range (3 kg at birth, 4 kg at 1 month and 7.89 kg at 12 months), but growth rate (both weight and height) significantly slows during the first two years of life, subsequently remaining steady. This results in final height values below the third percentile on the French standard growth curve [20], with a normal growth spurt at adolescence (30 cm) providing evidence that short stature in this population is not due to as the absence of a growth spurt during adolescence, as previously suggested. Median age at menarche was slightly late (14.5 years), with the first period occurring 2.5 years after the growth spurt, probably because of low levels of body fat. The youngest age at first pregnancy for Baka women was 16 years, and men seemed to begin reproducing later, as the youngest father were 20 years old. The Pygmy phenotype in the Baka may therefore result from a growth deficit in early infancy.

Biology of the somatotrophic axis

In 1981, Mérimée *et al.* described biological and hormonal explorations in adult Aka Pygmies from the Central African Republic [21]. The secretion of GH following stimulation, in the arginine test, was strictly identical to that of control subjects. However, the insulin response in the arginine or glucose perfusion tests was much weaker than that in controls and in subjects with GH deficiency. Baseline serum IGF I concentration was lower than that in controls, but higher than that in subjects with GH deficiency. By contrast, IGF II levels were within the normal range. Particularly marked hypoglycemia

was observed after intravenous insulin administration and the normalization of this hypoglycemia was slow. Moreover, treatment with GH (GH 5 mg/day for 3 days), which increased insulin secretion and decreased serum urea nitrogen levels in GH-deficient patients and controls, had no effect in Pygmies or on IGF I levels. Together, these results are consistent with resistance to GH. Merimee *et al* subsequently demonstrated abnormally low levels of GH-binding protein (GHBP), suggesting a smaller number of GH receptors (GHR), and suggested that this would be most consistent with a change in the regulation of *GHR* gene expression, rather than a structural defect of the coding sequence of the *GHR* gene [22,23]. These results were subsequently confirmed by the group of Bozzola *et al.* for the Baka group (Cameroon), which displayed baseline serum GH concentrations in the normal range, low serum GHBP concentrations, and extremely low levels of GHR expression. Conversely, IGF I levels were only moderately low [24].

Serum IGF I levels in Pygmy children (Ituri Forest, Zaire) have also been shown decreased during infancy, and any increase during adolescence was no more than moderate, consistent with the absence of a pubertal growth peak [16,25]. Western ligand blot analyses of IGF-binding proteins (IGFBP) have shown a very large decrease in IGFBP3 levels, with a slight increase during the pubertal period, associated with an increase in IGFBP2 levels [25]. The IGF1/IGFBP3 molar ratio, which provides insight into IGF I availability, was not studied during these periods.

Geffner *et al.* reported severe IGF I resistance in T-lymphoblast cell lines derived from Efe Pygmies [26]. The nucleotide sequence of the IGF type 1 receptor was normal, but receptor expression and function were poor in these immortalized African Pygmy T cells [27]. This is surprising, because serum IGF I levels would be expected to be high given the feedback regulation, whereas it has been shown to be low by various studies on these same populations of pygmies [16].

Genetic variants

Southern blots have shown an absence of *IGF 1* gene deletion in Pygmy populations. An RFLP-based study of polymorphisms (with *Hind* III/*Pvu*II, *Bst*NI and *Eco*RV) showed allelic frequencies very different from those in Caucasian populations, but very similar between the various Pygmy populations

(Central African Republic, Zaire, Melanesia) and relatively close to those of African non-pygmy black populations [28,29]. Sequencing of a portion of the *IGF 1* gene (300 bp immediately upstream from the *IGF 1* start site) revealed an absence of variation relative to control subjects, but it cannot be concluded from these findings that this gene plays no role in the short stature of Pygmies, as claimed by the authors of this study [28]. Our studies of the 5' non-coding region of the *IGF1* gene have revealed the presence of a nucleotide polymorphism at the Kozak consensus sequence [30], which is located just downstream from one of the ATG sites potentially used to initiate translation [31,32]. The variant identified in Pygmies may decrease translation efficiency, but it was also found in Caucasian subjects of small and normal stature [32].

Other genetic abnormalities may account for the small size of the pygmies. Low levels of insulin-like growth factor 1 and the lack of stimulation by growth hormone suggest possible deficiencies of growth hormone receptor (GHR) or of the GHR signaling pathway. Bozzola *et al.* reported normal basal serum GH levels associated with low serum GHBP and IGF I levels. They also reported low levels of GHR expression in peripheral blood cells, with no *GHR* DNA sequence variants [24]. Bauman *et al* and Merimee *et al* showed that levels of growth hormone binding to the high-affinity plasma GHBP were significantly lower in Pygmies than in controls, a finding consistent with the presence of a smaller number of GHR. Changes in expression due to alterations of the regulatory regions in either the 3' or 5' non-coding regions provide a more likely explanation for these findings than a structural abnormality in the coding sequence [22, 23, 33].

Becker *et al.* investigated the involvement of four candidate genes (*GHR*, *IGF1*, and the signal transducer and activator of transcription genes *STAT5A* and *STAT5B*) in the short stature of African pygmies, using a population genetics approach and phenotypic data. No significant genetic distances were found for the *STAT5A* and *STAT5B* genes. One of the polymorphisms considered, the deletion of *GHR* exon 3, was not found to be significantly more frequent in Baka pygmies than in their non-pygmy neighbors, the Nzime. However, this study revealed that the *GHR* and *IGF1* genes had experienced divergent natural selection pressures in Pygmies and non-Pygmies, throughout evolution. In addition, the SNPs considered (one in *GHR* intron 1 and the other in *IGF1* intron 2) were associated with stature

[18]. These results demonstrate the probable involvement of the GH–IGF1 axis in the difference in stature between African pygmies and their non-Pygmy neighbors, and confirm the associations found in a genome-wide study between loci involved in insulin and GH/insulin-like growth factor signaling [34]. Moreover this approach identified several genomic regions with strong signals of selection and association, some of which contained candidate genes for height variation. These regions included, in particular, one region of chromosome 3 harboring strong signals of natural selection and displaying differentiation between populations and association with height. This region also was also significantly associated with height in Europeans and contains a candidate gene known to regulate growth hormone signaling [34].

Discussion and Conclusion

The small size of Pygmies has long puzzled many researchers anthropologists, ethnologists, biologists, and geneticists. In addition to possible genetic causes, numerous evolutionary hypotheses have been proposed to explain the short stature of Pygmies, including adaptations to food scarcity, the difficulties of thermoregulation in a hot and humid environment, dense forest environments impeding mobility, or to a trade-off between growth cessation and age at first reproduction due to a high mortality rate [5]. Indeed, smaller bodies can survive with less food and can move around more easily in the rainforest. They are also adapted to hunting and gathering, and to thermoregulation in warm, moist tropical rainforests. Nutrition and infection are known to be involved in regulation of the GH/IGF1 axis [35, 36]. However, Froment *et al.* has shown that Pygmies obtain sufficient nutritional resources in forests, with a diet rich in protein and fiber and low in fat, with possible exchanges with non-Pygmy populations for other resources. Their daily diet generally contains 1800-1900 kcal [37, 38]. As far as infections are concerned, the non-Pygmy Bantu populations living in the same areas are subject to the same exposure to parasites, viruses, malaria, sickle cell anemia, hepatitis and other infectious risks [37, 38].

Despite the large amounts of clinical, biological, and molecular data on the somatotrophic axis now amassed, the enigma of the small size of Pygmy populations remains incompletely explained. In particular, doubts remain concerning the normality of or slight decrease in birth parameters in these populations, information important for guiding the identification of possible genetic defects. Further

studies of a larger number of Pygmy neonates are required, taking into account the specific locations of the populations concerned. The normality of GH levels, and the decrease in serum GHR and IGF1 levels in Pygmy populations are well established. Certain candidate genes, such as those encoding the GHR or its signaling molecules, appear to be involved, but other genes and their regulatory regions should probably also be analyzed with high-throughput genetic techniques, to improve our understanding of this extreme variation of size. Finally, epigenetic abnormalities may also be involved and should be investigated further.

Funding

Annual public funding from Inserm and UMPC-Paris6 University (IGFteam of the St-Antoine research center UMRS938)
ANRfunding-White Program “GrowinAP” (GrowthinAfrican Pygmies 2011–2015:PI FernandoRamirezRozzi).

Disclosure of interest The author declares that he has no competing interest

References

- 1- Cavalli-Sforza LL, editor. African Pygmies. London, Academic Press; 1986, p 1- 462.
- 2- Cavalli-Sforza LL. Pygmies, an example of hunter-gatherers, and genetic consequences for man of domestication of plants and animals. in: Proceedings of the 4th International Congress of Human genetics. Amsterdam: Excerpta Medica ;1971.
- 3- Bahuchet S. History of the inhabitants of the central African rain forest: perspectives from comparative linguistics. In: Hladik CM, Hladik A, Linares OF, Pagezy H, Semple A, Hadley M, editors. Tropical forests, people and food: biocultural interactions and applications to development. Paris/Lancs: Unesco/Parthenon;1993:37–54.
- 4- Froment A. Biological variation and adaptation in humans: the case of African pygmies. Bulletin et Mémoires de la Soc Anthropol Paris; 1993;5:417–448.
- 5- Becker NS, Verdu P, Froment A, Le Bomin S, Pagezy H et al . Indirect evidence for the genetic determination of short stature in African Pygmies. Am J Phys Anthropol. 2011;145(3):390-401.
- 6- Becker N. La faible stature des populations pygmées d'Afrique centrale : une approche évolutive [thèse]. Paris : Université Pierre et Marie Curie-Paris VI; 2012. p.1-168
- 7- Verdu P, Becker NS, Froment A, Georges M, Grugni V, *et al* Sociocultural behavior, sex-biased admixture, and effective population sizes in Central African Pygmies and non-Pygmies.

- Mol Biol Evol. 2013 Apr;30(4):918-37. doi: 10.1093/molbev/mss328. Epub 2013 Jan 7.
- 8- Pick P. Au commencement était l'homme, de Toumaï à Cro-Magnon. in: Odile Jacob Ed: Paris.2003: p 9-256
- 9- Patou6-Mathis M. Néanderthal une autre humanité.In: Perrin Ed, Paris. 2010: p7-365
- 10- Quintana-Murci L, Quach H, Harmant C, Luca F, Massonnet B, *et al*
Maternal traces of deep common ancestry and asymmetric gene flow between Pygmy hunter-gatherers and Bantu-speaking farmers.
Proc Natl Acad Sci U S A. 2008 Feb 5;105(5):1596-601.
- 11- Verdu P, Austerlitz F, Estoup A, Vitalis R, Georges M, *et al*
Origins and genetic diversity of pygmy hunter-gatherers from Western Central Africa.
Curr Biol. 2009 Feb 24;19(4):312-8. doi: 10.1016/j.cub.2008.12.049. Epub 2009 Feb 5.
- 12- Patin E, Laval G, Barreiro LB, Salas A, Semino O, et al Quintana-Murci L. Inferring the demographic history of African farmers and pygmy hunter-gatherers using a multilocus resequencing data set.
PLoS Genet. 2009 Apr;5(4):e1000448. doi: 10.1371/journal.pgen.1000448. Epub 2009 Apr 10
- 13- Perry GH, Dominy NJ: Evolution of the human pygmy phenotype. Trends Ecol Evol 2009; 24: 218–225.
- 14- Vincent, M., Jans, C. , Ghesquiere, J., 1962, The new-born Pygmy and his mother. American Journal of Physical Anthropology, 20, 237-247.
- 15- Bailey RC.
Growth of African Pygmies in early childhood.
N Engl J Med. 1990 Oct 18;323(16):1146
- 16- Merimee TJ, Zapf J, Hewlett B, Cavalli-Sforza LL.
Insulin-like growth factors in pygmies. The role of puberty in determining final stature.
N Engl J Med. 1987 Apr 9;316(15):906-11.
- 17- Bailey RC.
The comparative growth of Efe pygmies and African farmers from birth to age 5 years. Ann Hum Biol. 1991 Mar-Apr;18(2):113-20.
- 18- Becker NS1, Verdu P, Georges M, Duquesnoy P, Froment A, et al
The role of GHR and IGF1 genes in the genetic determination of African pygmies' short stature.
Eur J Hum Genet. 2013 Jun;21(6):653-8. doi: 10.1038/ejhg.2012.223. Epub 2012 Oct 10.
- 19- Rozzi FV, Koudou Y, Froment A, Le Bouc Y, Botton J.
Growth pattern from birth to adulthood in African pygmies of known age.
Nat Commun. 2015 Jul 28;6:7672. doi: 10.1038/ncomms8672.

20-Sempé G, Pédrón G, Roy-Pernot MP. Auxologie, Méthode et Séquences. Paris, Laboratoire Théraplix; 1979.

21- Merimee TJ, Zapf J, Froesch ER.
Dwarfism in the pygmy. An isolated deficiency of insulin-like growth factor I.
N Engl J Med. 1981 Oct 22;305(17):965-8.

22- Merimee TJ, Hewlett BS, Wood W, Bowcock AM, Cavalli-Sforza LL.
The growth hormone receptor gene in the African pygmy.
Trans Assoc Am Physicians. 1989;102:163-9

23- Merimee TJ, Baumann G, Daughaday W.
Growth hormone-binding protein: II. Studies in pygmies and normal statured subjects.
J Clin Endocrinol Metab. 1990 Nov;71(5):1183-8.

24- Bozzola M, Travaglino P, Marziliano N, Meazza C, Pagani S, *et al*
The shortness of Pygmies is associated with severe under-expression of the growth hormone receptor.
Mol Genet Metab. 2009 Nov;98(3):310-3. doi: 10.1016/j.ymgme.2009.05.009. Epub 2009 May 28.

25- Hardouin S, Gournelen M, Noguiez P, Seurin D, Roghani M, *et al*
Molecular forms of serum insulin-like growth factor (IGF)-binding proteins in man: relationships with growth hormone and IGFs and physiological significance.
J Clin Endocrinol Metab. 1989 Dec;69(6):1291-301.

26- Geffner ME, Bersch N, Bailey RC, Golde DW.
Insulin-like growth factor I resistance in immortalized T cell lines from African Efe Pygmies.
J Clin Endocrinol Metab. 1995 Dec;80(12):3732-8.

27- Hattori Y, Vera JC, Rivas CI, Bersch N, Bailey RC, *et al*
Decreased insulin-like growth factor I receptor expression and function in immortalized African Pygmy T cells.
J Clin Endocrinol Metab. 1996 Jun;81(6):2257-63.

28- Bowcock A, Sartorelli V.
Polymorphism and mapping of the IGF1 gene, and absence of association with stature among African Pygmies.
Hum Genet. 1990 Aug;85(3):349-54

29- Schneid H, Le Bouc Y, Seurin D, Gournelen M, Cabrol S, *et al*
Insulin-like growth factor-I gene analysis in subjects with constitutionally variant stature.
Pediatr Res. 1990 May;27(5):488-91.

30- Kozak M.
Point mutations close to the AUG initiator codon affect the efficiency of translation of rat preproinsulin in vivo.
Nature. 1984 Mar 15-21;308(5956):241-6.

31- Schneid H, Seurin D, Le Bouc Y.

- Pathology of the growth and abnormalities of IGF genes.
Ann Endocrinol (Paris). 1991;52(6):479-82. Review. French.
- 32- Schneid H. Etude des gènes des insulin-like growth factors (IGF I et IGF II) dans des anomalies de croissance [thèse]. Paris : Université Pierre et Marie Curie-Paris VI; 1990. p.1-189
- 33- Baumann G1, Shaw MA, Merimee TJ.
Low levels of high-affinity growth hormone-binding protein in African pygmies.
N Engl J Med. 1989 Jun 29;320(26):1705-9.
- 34- Jarvis JP, Scheinfeldt LB, Soi S, Lambert C, Omberg L, *et al*
Patterns of ancestry, signatures of natural selection, and genetic association with stature in Western African pygmies.
PLoS Genet. 2012;8(4):e1002641. doi: 10.1371/journal.pgen.1002641. Epub 2012 Apr 26.
- 35- Thissen JP, Ketelslegers JM, Underwood LE.
Nutritional regulation of the insulin-like growth factors.
Endocr Rev. 1994 Feb;15(1):80-101. Review.
- 36- Thissen JP, Verniers J.
Inhibition by Interleukin-1 β and Tumor Necrosis Factor- α of the Insulin-Like Growth Factor I Messenger Ribonucleic Acid Response to Growth Hormone in Rat Hepatocyte Primary Culture.
Endocrinology. 1997 Mar 1;138(3):1078-1084.
- 37- Froment A, Garine I de, Binam Bikoi Ch, Loung JF. Bien manger et bien vivre in : Orstom-l'Harmattan, Ed. Antropologie alimentaire et développement en Afrique intertropicale, du biologique au social. Paris;1996: p271-288
- 38- Froment A. Evolutionary biology and health of hunter-gathered populations. In : Panter-Brick C, Layton R, Rowley-Conwy, Eds."Hunter-gatherers : an interdisciplinary perspective", Cambridge University Press; 2001: 239-266.