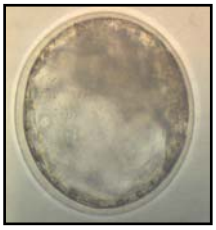

ASSOCIATION EUROPEENNE DE TRANSFERT EMBRYONNAIRE

A.E.T.E. NEWSLETTER N°29

June 2008 **Editor: Alfonso Gutiérrez-Adán**

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A.E.T.E. Newsletter
Alfonso Gutiérrez-Adán, Editor
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Web Site: http:// www.aete.eu
Letters to the Editor are welcomed.
Please include name, address,
telephone, FAX, and E-mail address

President's letter

Dear Collegues

The 24th scientific meeting of the AETE will be held on the 12th and 13th of September 2008 in Pau, a beautiful town of south-western France with magnificent views of the Pyrénées Mountains. The meeting will take place at the Palais of Congrés, a luxurious palace that will certainly offer a special and sumptuous atmosphere for our Association. Please visit the AETE web site (www.aete.eu) for more detailed in formations about Pau and travel information.

Four invited lectures will be at the centre of the scientific programme and will cover topics such as embryo-maternal interactions and embryo-pathogen interactions followed by an update on semen sexing together with a final lecture about the generation of recombinant antibodies from transgenic farm animals.

Two workshops are included in the programme about animal cloning and products from cloned animals, and assisted reproduction and genetic selection in beef cattle. The second workshop will be followed by a special dinner on Saturday evening that is an addition the the social programme for this year. Workshop organisers are working hard to make sure that several members will actively contribute to make these events truly

European with the participation of scientists and practitioners from different countries.

Four oral presentations have been selected for the Student Competition section as a result of a selection from the seven that have been submitted to the Board. The choice of the top four has been quite difficult because of the very high overall scientific quality. All seven have been accepted for poster presentation and are included in the poster session that completes the programme. Also this year over 60 posters have been submitted and most have been accepted and included in the proceedings. Several different species and topics are addressed and, for this reason, the poster session will offer a variety of subjects for discussion and exchange of informations and ideas.

I would like to express my warmest thanks to the members of Local Organising Committee in Pau for taking care of the logistics and for devoting a lot of their time and efforts to make sure that our stay in Pau will be enjoyable and the meeting will be successful. Special thanks go also to our sponsors that have generously provided the financial support to allow the meeting to take place, therefore supporting both the science and the practice of embryo transfer and related technologies in Europe.

Finally, I would like to invite all members of our Association and all colleagues working in the embryo transfer field to join the 2008 meeting in Pau and to provide their input and contributions to the activities of the AETE.

Giovanna Lazzari
President A.E.T.E. June 2008

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PRESS AND NEWS ROOM

Paternal effect on embryo quality in diabetic mice is related to poor sperm quality and associated with decreased GLUT expression. ST Kim and K Moley. Reproduction Advance Publication (16 June 2008).

Mammalian embryos are vulnerable to injury during the pre-implantation stages of development. Glucose transport and metabolism are critical for blastocyst formation and further development. To analyze if sperm quality, fertilization capacity, and subsequent embryo development are altered in diabetic male mice and if differences in facilitative glucose transporter (GLUT) expression in testis and sperm exist; the authors used two type 1 diabetic mouse models. GLUT1, 3 and 5 did not change in expression in the testes or sperm between diabetic and non-diabetic mice. GLUT8 and GLUT9b were less expressed in testes of both diabetic models vs controls. GLUT9a was not expressed in the Akita testis or sperm as compared to strain-matched controls. 3β-HSD expression was significantly decreased in the Leydig cells from the diabetic mice. Sperm concentration and motility were significantly lower in both the diabetics as compared to the control. Theses parameters normalized in Akita diabetic males treated with insulin. In addition, fertilization rates were significantly lower in the Akita group (17.9%) and the streptozotocin (STZ)-injected male group (43.6%) as compared to the normal group (88.8%). Interestingly, of the fertilized zygotes, embryo developmental rates to the blastocyst stage were lower in both diabetic models (7.1%-Akita and 50.0%-STZ) as compared to controls (71.7%). Male diabetes may cause male subfertility by altering steroidogenesis, sperm motility and GLUT expression. This is the first study to link a paternal metabolic abnormality to a sperm effect on cell division and subsequent embryonic development.

Dr Alfonso Gutiérrez-Adán
INIA, Madrid, Spain

The ground state of embryonic stem cell self-renewal Ying QL, Wray J, Nichols J, Batlle-Morera L, Doble B, Woodgett J, Cohen P, Smith A. Nature 2008;453(7194):519-23.

The culture requirements of mouse embryonic stem (ES) cells have been known from several years and are based on various combinations of feeders, cytokines, growth factors, generally with the addition of serum. These are all complex culture conditions that have not allowed to fully dissect the basic requirements for maintaining the undifferentiated state in vitro. In this paper the authors provide full evidence that the precise block of signalling pathways that induce differential is sufficient to maintain the undifferentiated state in absence of specific growth factors such as LIF or BMP4, known to sustain the ES state. The authors show that mouse ES cells can be derived and propagated in absence of exogenous stimuli (serum and/or growth factors) by eliminating the autocrine differentiation-inducing activity of specific mitogen-activated protein kinases. This is achieved by using selective small-molecule inhibitors SU5402 or PD173074 and PD184352 to inhibit FGF receptor tyrosine kinases and the ERK cascade, respectively. The inhibitors can be used in combination with LIF, in serum free medium, or in absence of LIF. In this latter case, however, cell viability is low and a third small molecule, CH99021, an inhibitor of glycogen synthase kinases 3 (GSK3), is required to increase viability and allow cell replication. Newly derived ES cell lines in these conditions (3i medium) give rise to germ line chimeras after blastocyst injections therefore confirming the full set of ES properties. The authors therefore propose that the ES cell state is a basal condition that can be maintained simply by blocking the autocrine differentiation stimuli. The same approach is expected to allow ES cell derivation in other species, perhaps including farm animals where ES cells are still elusive.

Dr Giovanna Lazzari
CIZ, Cremona, Italy

The 24th Scientific Meeting of the A.E.T.E

will be held in

Pau - France

12TH - 13TH SEPTEMBER 2008

Invitation

On behalf of the European Embryo Transfer Association the local organizing committee cordially invites you to the 24th scientific meeting of the organization in Pau, France, from the 12th to the 13th of September 2007.

We are glad to found in Pau a very nice location in the Pyrenees. From humble beginnings as a crossing on the Gave de Pau ("Gave" roughly translates as valley) for flocks en route to and from the mountains, PAU became the capital of the ancient viscountcy of Béarn in 1464, and of the French part of the kingdom of Navarre in 1512. In 1567 its sovereign, Henri d'Albret, married the sister of the king of France, Marguerite d'Angoulême, friend and protector of artists and intellectuals and herself the author of a celebrated Boccaccio-like tale (the Heptameron), who transformed the town into a centre of the arts and nonconformist thinking.
Official Website: http://www.ville-pau.fr/

The meeting will take place in the Conference Center of the Palais Beaumont (Pau). The Conference Center offers a prestigious environment, and can provide all the services we need for the AETE Meeting. The Palais Beaumont is now a member of the Historic Conference Centre of Europe alliance.

How to come to Pau
1) Plane Pau Airport
20 minutes from the Palais Beaumont
Daily flights
- 9 to Paris
- 3 to Lyon
- 1 to London
Tel +33 (0)559 333 300
2) Train TGV Train Station
5 minutes on foot via the famous cable car
Tel +33 (0)836 353 535
3) Road 10 minutes from:
A64 - La Pyrénéenne, Toulouse - Biarritz
Exit Pau Centre
RN 134 - Bordeaux - Pau - Oloron - Espagne

Language
The official language of the conference is English.

Scientific Secretariat
AETE board

Organising Secretariat

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Preliminary Scientific program

- Pascale Chavatte (fetal maternal interactions)
- Ann Van Soon (embryo-pathogen interactions)
- Detlef Rath (semen sexing update)
- Gottfried Brem (title to be confirmed)
- Yvan Heyman (workshop on cloning and products from cloned animals)
- Serge Lacaze (workshop on assisted reproduction and selection in beef breeds)
- Gottfried Brem (Pioneer Award)
- Eckard Wolf (laudatio to Pioneer Award)

The final scientific program is included in this Newsletter.

REGISTRATION FEES

Pau 2008	Euros
Full/Associate Member Before *15th July 2008*	200€
Full/Associate Member After *15th July 2008*	250€
Student Member Before *15th July 2008*	140€
Student Member After *15th July 2008*	155€
2008 Membership Fee *Members who pay their annual fee but do not attend the Meeting will receive a copy of the proceedings*	70€

This price includes:

- participation at the Meeting (two full days)
- two workshops
- published proceedings
- lunch and coffee breaks

Fees for Sponsoring AETE Meeting

Main Sponsor	7 500 Euros
General Sponsor	4 500 Euros
Exhibitors	1 900 Euros

Costs for advertisement in the Newsletter (2 issues) for one year: mailed to 700 members

Full color back page	800 Euros
Full inside color page	600 Euros
Half inside color page	400 Euros

A.E.T.E. ASSOCIATION EUROPEENNE DE TRANSFERT EMBRYONNAIRE
EUROPEAN EMBRYO TRANSFER ASSOCIATION

24th SCIENTIFIC MEETING

„Palais Beaumont “
PAU, FRANCE

P R O G R A M M E

12th and 13th September 2008

Thursday, September 11th 2008

19:00: **Welcome Reception - Palais des Congrès**

FRIDAY, September 12th 2008

07:30-09:00: Registration

09:00-09:10: Opening meeting by President **Giovanna Lazzari**

SESSION 1 – Chairpersons: Alfonso GUTIERREZ-ADAN & Ian KIPPAX

09:15-10:00: **First invited lecture:**
„Fetal maternal interactions“
(Pascale Chavatte-Palmer, France)

10:00-10:45: **Short oral communications**
(1) HOELKER M et al.,: Gene expression differences between bovine embryo biopsies derived from blastocysts resulted in different pregnancy outcomes after transfer to recipients.
(2) GONZALEZ C et al.: Pregnancy rates after single direct transfer of biopsied frozen-thawed bovine embryos according to quality.
(4) AYAD A et al.: Effect of parity on pregnant associated glycoprotein (pags) levels measurement by radioimmunoassay in bovine. Preliminary results.

10:45-11:05: **Short Sponsor Presentation** (á 5 minutes: PFIZER, BIONICHE, CALIER, CEVA)

11:05-12:00: POSTER SESSION 1 and coffee break

12:00-13:00: Lunch

SESSION 2 – Chairpersons: Sybrand MERTON & Serge LACAZE

13:00-13:45: **Second invited lecture:**
„Semen sexing update“
(Detlef Rath, Germany)

13:45-15:00: **Short oral communications (Student Competition)**
(1) CLEMENTE M et al.: Effect of exogenous progesterone in vitro on the quality of bovine blastocysts on Day 7 and Day 14.
(2) MAREI WF et al.: Effects of linolenic acid on bovine oocyte maturation and early embryo development in vitro.
(3) MUGNIER S et al.: Comparison of the composition and morphology of the Zona Pellucida of equine and porcine oocytes.
(4) BOURDIN P et al.: Retrospective study of factors of variation of the superovulation response in Midatest embryo transfer team.

15:00-16:00: POSTER SESSION 2 and coffee break

16:00-17:30: **Workshop I – „Animal cloning and products from cloned animals“**
(Coordinator: **Yvan Heyman, France**)

18:00: Guided tour of the Henry VI castle
20:00 : **Social Event** - Gala dinner in the Palais Beaumont ("Salle des Ambassadeurs")

SATURDAY, September 13th 2008

SESSION 3 – Chairpersons: Claire PONSART & Peter VOS

09:00-09:45: **Third invited lecture:**
„Embryo-pathogen interactions“
(Ann Van Soom, Belgium)

09:45-10:30: **Short oral communications**
(1) LACAZE S et al.: A potential contamination of the biopsy by Zona Pellucida associated y DNA does not affect embryo sexing results.
(2) LI J et al.: Production of porcine chimeric embryos with aggregation of embryos or blastomeres.
(3) MERTON JS et al.:Effect oocyte collection method and breed on efficiency of oocyte collection and subsequent in vitro bovine embryo production.

10:30-11:00: **General Assembly**

11:00-11:30: **Coffee break**

11:30-12:15: **Short oral communications**
(1) SLEZAKOVA M et al.: The relationship between the number of CL and embryo quality.
(2) KARADJOLE M et al.: Comparison of bovine oocyte recovery and *in vitro* embryo development after ovum pick up in simmental, charolais and holstein friesian cows.
(3) POSADO R et al.: DNA fragmentation in frozen semen samples of fighting bulls.

12:15-13:15: Lunch

SESSION 4 – Chairpersons: Frank BECKER & Urban BESENFELDER

13:15-14:00: **Fourth invited lecture:**
“Generation of Recombinant Antibody Transgenic Farm Animals“
(Gottfried Brem, Germany)

14:00-14:30: **AETE Medallist Presentation: Gottfried Brem (Germany)**
(Introduced by **Eckhard Wolf, Germany**)

14:30-14:45: **Short Sponsor Presentation** (á 5 minutes**:** INTERVET, MERIAL, ULG Liège)

14:45-15:45: POSTER SESSION 3 and coffee break

15:45-17:15: **Workshop II – „Assisted reproduction and genetic selection in beef breeds“**
(Coordinator: **Serge Lacaze, Patrice Humblot, Claire Ponsart** France)

17:15-17:30: Closing session, Student Competition results and invitation to 2009 Meeting

18:00: Visit of the MIDATEST Station followed by a typical dinner in Jurançon with wine and regional products degustation (transport by bus provided)

TELOMERE LENGTHENING DURING PREIMPLANTATION DEVELOPMENT

E Pericuesta, MA Ramírez, R Fernández-González, M Pérez-Crespo, JD Hourcade, P Bermejo, D Rizos, and A Gutiérrez-Adán. Department of Animal Reproduction, INIA, Madrid, Spain

For most cell types, each cell division results in the shortening of chromosomes length. The terminal ends of chromosomes, which are known as telomeres, are critical for maintaining chromosome stability, proper segregation of chromosomes and ensuring the full replication of coding DNA through meiotic cell division. During replication conventional DNA polymerases cannot replicate the extreme 5´-ends of chromosomes, and as a result, telomere is shorter and cell cycle is arrested. To counteract this end-replication problem, some cell types express the enzyme telomerase. Telomere repeats are generated by a cellular reverse transcriptase known telomerase (Telomerase reverse transcriptase, Tert). Telomerase recognizes the 3´-OH at the ends of chromosomes and adds telomere repeats de novo by using an associated RNA molecule as a template (Telomerase RNA component, or Terc). Multicellular eukaryotes have limited amounts of telomerase, and telomere shortening occurs coupled to cell division owing to the incapacity of normal DNA polymerases to copy the very ends of chromosomes. This phenomenon is not observed in immortal cells where telomere length is maintained by the transcriptase reverse telomerase enzyme which synthesizes telomere repeats on the end of eukaryotic chromosomes. Furthermore, high telomerase activity has been described in germ, embryonic and cancer cells, whereas most somatic cells show a low or inexistent telomerase activity.

Sperm maintain lengthy telomeres, but mammalian oocytes have short telomeres [1]; however, by the two-cell stage, the length of the telomeres increase [1], and the stimulus for this growth did not come from the sperm, because telomeres extended even in oocytes developing parthenogenetically. The enzyme telomerase is active in germ cells and during early embryogenesis [2] and is crucial for the maintenance of telomere length and germ cell viability in successive generations of a given species [3]. The establishment of telomere length during embryogenesis could determine telomere reserves in newborns. In mTERC-/- mouse embryos, telomeres are not elongated, indicating that the telomerase enzyme is required for telomere elongation during early embryogenesis. Recently it has been analyze telomere length at different stages of bovine and mouse early development employing embryos derived from nuclear transfer, IVF, and normal breeding, and they have found that telomere length is determined at morulae to blastocyst transition by a telomerase-dependent mechanism [4]. However, other reports from cow [5] and human [6] studies have demonstrated that telomerase activity can be detected in all developmental stages starting form immature oocytes through the blastocyst stage. Contrary to what other authors have shown, Liu et al. have recently reported that telomerase activity is very low in oocytes and early embryos, and that telomerase contributed little to embryonic development before blastocysts stage [1], even with no telomerase activity, the authors saw lengthening of the telomeres during early development. Using telomere quantitative fluorescent in situ hybridization, the authors found that mature oocytes had short telomeres (shorter than in somatic cells), and that telomeres lengthened remarkably in one- to two-cell stage mice embryos; suggesting that early embryos rapidly extend their shrunken telomeres mainly through recombination between the tips of sister chromatids. There are two DNA repair proteins (Rad50 and BLN) in the nuclei of early embryos that they could be mending telomeres after recombination. At blastocyst stage, when there is expression of telomerase, the telomere lengthening is then mediated by the telomerase. Telomeres do not elongate appreciably after the blastocyst stage [4], however many tissues from fetal or adult mice exhibit high telomerase activity. This may indicate that telomere length is established during early preimplantation development, and that the activation of telomerase in blastocysts only preserves telomere length during later development.

Telomere length in cloned and manipulated embryos

In animals produced by somatic cell nuclear transfer (SCNT) and in vitro embryo production an increased pre- and perinatal mortality has been found as a consequence of several abnormalities, such as extended gestation length, oversized offspring, aberrant placental development, cardiovascular and respiratory problems, immunological deficiencies, problems with tendons, adult obesity, kidney and hepatic malfunctions, behavioural changes, and a higher susceptibility to neonatal diseases. Several epigenetic alterations have been associated with in vitro embryo production techniques and SCNT and provide a link between these procedures and the abnormalities found. Telomere elongation during embryogenesis could be critical to ensure normal telomere length in the offspring, as no telomere elongation occurs after the blastocyst stage, and could have direct effects on carcinogenesis, regeneration and ageing during postnatal life.

Manipulated embryos

The rate of telomere erosion and incidence of chromosome abnormalities may affect developmental potential of early embryos and may be potential predictors of developmental outcome. In vitro fertilization (IVF) and intracytoplasmatic sperm injection (ICSI) are considered safe technologies both in animals and in humans, but several abnormalities related to these techniques have been reported. There are evidences for increased pre-maturity and decreased birth weights in singleton babies and birth defects after IVF or ICSI [7, 8] and chromosome abnormalities after ICSI [9]. All these phenotypes have been related with epigenetic errors, such as X-Chromosome inactivation or telomere length modifications. As these changes are completed by the late blastocyst stage, these phenotype-related epigenetic alterations must have occurred during the preimplantation period. In this prospective, telomere length, methylation status and X-chromosome inactivation have been proposed as additional measure for the assessment of early embryo development quality in the context of assisted reproduction [10].

It has been reported in mice that ICSI has an effect on the telomere length [11]. Suboptimal in vitro culture conditions may also have some effect on gene expression and produce shorter telomeres and chromosome abnormalities at blastocyst stage. In bovine embryos, it was observed that the post-fertilization culture environment of the developing embryo can affect the incidence and the severity of mixoploidy in the resulting blastocyst [12, 13]. Also when mice embryos were cultured in vitro in media containing FCS a long term effect on the health of the adult offspring was observed [8, 14]. Microarray analysis have demonstrated that the expression of some genes related with telomere complex are affected by the IVC (data non-publish), and this may have a short term effect on the quality of the blastocysts, and also be related with a long term effect on the offspring. It has been reported in mice that the frequency of tumors and the duration of the life are affected by the ICSI protocol used [11]; both of these phenotypes are clearly related with the telomere length.

In bovine, no differences in telomerase activity in blastocysts were found between nuclear transfer (NT) embryos and IVF, but higher telomerase activity was found in parthenogenetic blastocysts [15]. Similarly, no differences in telomere length were found between SCNT or IVF-produced mouse and bovine embryos [16, 17]. In particular, Schaetzelein et al. analyzed at different stages telomere length in bovine and mouse embryos derived from somatic nuclear transfer, in vitro production (in vitro maturation, fertilization, and culture), and conventional breeding [17]. The observation that telomere elongation through telomerase occurs at the morula–blastocyst transition in embryos from both mammalian species as well as embryos derived from both in vivo or in vitro fertilization and even somatic nuclear transfer indicates a general program in preimplantation development. When telomere length was analyzed at morula stages, which are known to be telomerase negative or to possess minimum telomerase activity, similar telomere lengths were found in in vivo and in vitro produced embryos. This observation ruled out the possibility that the in vitro culture per se had a significant effect on telomere length. From morula to blastocyst stage telomeres were significantly

elongated in both SCNT and IVF embryos and no differences between both groups were found. In agreement, a strong up-regulation of telomerase was observed at the blastocyst stage as previously described in human, mice and bovine embryos [5, 6, 18], indicating that telomere elongation at this developmental stage is correlated with the timing of telomerase reactivation during embryogenesis.

Cloned embryos

In somatic cell nuclear transfer, an overall epigenetic reprogramming must occur to abolish the somatic cell expression profile and to establish a new embryo-specific expression profile. The epigenetic reprogramming involves processes such as DNA methylation, X-chromosome inactivation and adjustment of telomere lengths. Variations in DNA methylation [19], aberrant patterns of X inactivation [20], imprinted gene expression [21] and telomere lengths [22, 23] have been observed in the somatic cells of some SCNT clones which has led to speculation that incomplete genetic and epigenetic reprogramming of the donor cells could cause developmental irregularities and post-natal abnormalities [24].

Somatic differentiation implies a progressive shortening of telomeres, which raises the question of whether cloned animals inherit the shortened telomeres of the somatic cell. Since it was announced that Dolly the sheep might be aging faster than normal because her telomeres were shorter than age-matched control sheep [25, 26], many studies have analyzed telomere length and telomerase activity in cloned animals. When epigenetic marks are analyzed in cloned embryos, it is difficult to discriminate between effects of in vitro culture and the cloning process itself. However, similar telomere lengths were found in IVF-derived and in vivo morulaes, whereas in SCNT morulaes telomere length was shorter [17].

Telomere lengths in animal clones have been reported as being shorter [23, 25, 27, 28], no different [17, 22, 27, 29-34], and even slightly longer [23, 30, 35, 36] than in age-matched control animals. The possible explanations to the different telomere lengths observed among studies are differences in donor cell type [23], efficiency of telomerase reprogramming [22, 30], individual-to-individual variations [22], the nuclear transfer procedure [33, 35], the tissue/cell type analyzed [22, 35] and disparity among species [22, 25, 30, 33, 35]. Shortened telomeres were seen in the first cloned sheep, Dolly [25], but not in cloned calves [22, 32, 33], mice [36], pigs [30, 31, 34], goats [27] and dogs [29]. This fact may suggest specie-related differences in the telomere restoration mechanism after NT. However, there are growing evidences that telomere restoration in cloned animals depends on the donor cell type used in NT rather than in the specie since Miyashita et al. found that cattle cloned from fibroblasts or muscle cells content telomeres with a similar length to that of age-matched controls, while clones derived from epithelial cells, as it was used in Dolly, do not restore the normal telomere length [23]. A relationship between telomere length reprogramming and the donor cell type used was also reported in goats [27]. Another important aspect to be considered is the number of passages of the donor cells before the performance of the SCNT, since cellular division implies a progressive shortening of telomeres. In bovine, no difference in nuclear cloning efficiency was found when high-passage fibroblast was used compared to the use of low-passage cells [32, 37], but in sheep, cloning problems appear to increase with the passage number of the donor cells [25, 38-40].

Telomere length regulation in clones

In early embryos, telomere lengthening mechanism remains poorly understood. As it was mentioned previously, telomeres lengthen remarkably in one- to two-cell stage embryo when telomerase activity is low or absent in mice [1], human [41] and bovine [5, 18]. Furthermore, telomeres also elongate in the early cleavage embryos of telomerase-null mice demonstrating that telomerase is unlikely to be responsible for telomere lengthening before the blastocyst stage [1]. Therefore, an alternative recombination-based mechanism has been proposed as responsible of telomere lengthening during early cleavage until the morula/blastocyst transition [1]. Once the morula stage is reached, telomerase activity continues telomere lengthening, being essential to reach the normal telomere length [17]. From the blastocyst stage onwards, telomerase only maintains the telomere length already established

[17]. In conclusion, the action of two mechanisms (recombination-based and telomerase) on two different periods seems to be responsible for telomere length reset in normal embryos. However, the mechanism of telomere lengthening in SCNT embryos may differ from the normal embryo.

Currently, no study has been addressed to analyze the recombination-based mechanism in cloned embryos. Nevertheless, it seems that telomere reset in SCNT embryos occurs at the morula/blastocyst transition because SCNT bovine morula telomeres are shorter than in in vivo or IVF-derived morulas, while at the blastocyst stage, similar telomere length was found in both IVF-derived and SCNT [17]. The elongation process at this stage seems to be telomerase dependent, as it was abrogated in telomerase deficient mice [17]. In agreement, a higher telomerase activity was observed in porcine SCNT blastocysts compared to IVF-derived blastocysts [30]. On the other hand, it has been proposed that, rather than telomere restoration, cloned animals may be derived from the selective propagation of cells with enhanced telomere reserves during the cloning process and/or early embryonic development, which would be consistent with the low efficiency of somatic cloning [42].

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ANNOUNCEMENT:

12th ESDAR Conference & Annual Meeting of EU AI-Vets

November 20th-23rd, 2008

Educatorium Universiteit Utrecht, de Uithof, The Netherlands

FBU Conference Office, Ms. Odette Jansen
E-mail: esdar-aivets2008@uu.nl, Phone: +31 30 253 2728

www.esdar.org

American Embryo Transfer Association (AETA) & Canadian Embryo Transfer Association (CETA/ACTE)

October 16-18, 2008

2008 Joint Scientific Convention
Kansas City, Missouri, USA

For more information and the program outline, please visit:
http://www.ceta.ca/08convention.htm
or contact the CETA/ACTE office at: Email: ceta@ebi.ca

A.E.T.E. ASSOCIATION EUROPEENNE DE TRANSFERT EMBRYONNAIRE
EUROPEAN EMBRYO TRANSFER ASSOCIATION

24th AETE meeting, September 12th to 13th, PAU 2008

Office de Tourisme et des Congrès

Pau la vie rêvée des villes

HOTEL RESERVATION

We kindly ask each participant to complete the following hotel booking form and to read the specific conditions relative to the hotel reservation.

The rooms will be assigned by the **Office du Tourisme et des Congrès** according to the choices of the participants (please see above the list of the possible hotels) and the date of receipt of the hotel booking form.

Name of the pre-booked hotels	Localisation	Rooms Availability	single room* *(1 breakfast inclued)*	double room* *(2 breakfasts inclued)*	free parking
3 Stars					
1.Kyriad centre	City-Center	50	108 €	120 €	Yes
2.Gramont	City-Center	18	95 €	109 €	No
3.Continental	City-Center	30	71 to 84	92 to 112	Yes
4.Le Roncevaux	City-Center	20	86 €	96 €	Yes
5.Le Montpensier	City-Center	14	87 €	95 €	No
2 Stars					
6.Bourbon	City-Center	10	65 €	82 €	No
7.Bosquet	City-Center	25	69 €	81 €	No
8.Ibis	City-Center	40	70 €	79 €	Yes

* Booking fees and staying taxes are included in the prices

For any information about tourism possibilities in Pau and its region, we invite you to visit the following website : www.pau-pyrenees.com

For any request concerning the hotel reservation, please contact :

Françoise LAMARQUE, Service reservation
Office de Tourisme et des Congrès de Pau / AU064960001
Place Royale, 64 000 PAU, France
Tel : 00 33 5 59 27 17 49 - Fax : 00 33 5 59 27 66 63 - Mail : omt.service-groupe@pau.fr
Internet website:www.pau-pyrénées.com

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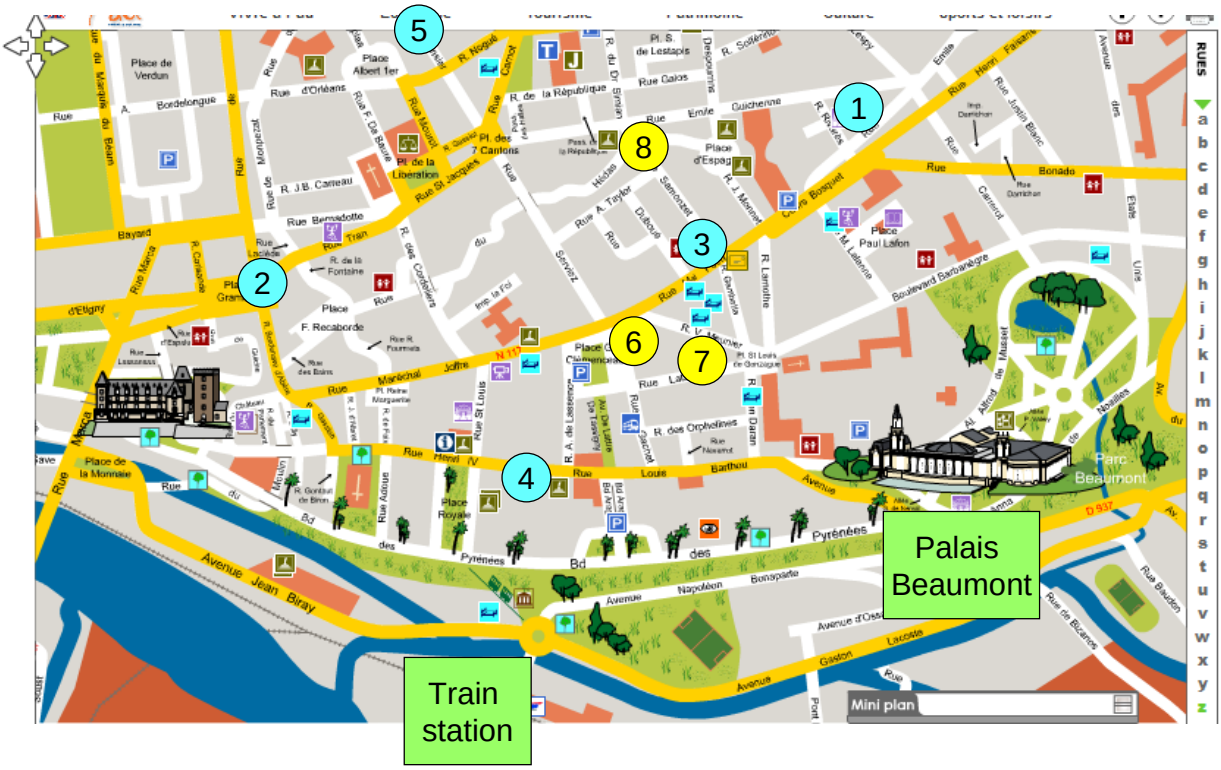
Hotels localisation – Map of Pau



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HOTEL BOOKING FORM

NAME : …… **SURNAME :** ……

Phone Number : ……**E.mail address:** ……

Full mailing address :
……

Postal code : ……... **City :** …… **Country :** ……

COMPANY :……

BOOK YOUR HOTEL (breakfast included)

Hotel Name : 1st choice …… **2d choice** ……

Number of persons :…….. **Number of SGL rooms:** ……..

Number of DBL rooms :……. **Number of TWIN rooms (2 beds):** ……

I wish to share the room with :……

Night of Thursday 11th sept ☐ **Night of Friday 12th sep** ☐
Night of Saturday 13th sept ☐

Extra Nights :…… Dates:……

PAYMENT (after receiving invoice) : ☐ Cheque ☐ Bank transfer ☐ Credit card

If payment by card : Card number ……
Expiration date (mm/yy) : ……Cryptogram :……
(last 3 numbers on the back of the card)

I declare that I have read and do here by agree to the conditions of booking

Date and Company :

Booking form to send back (E-mail or fax) before July 1st 2008 to :

Françoise LAMARQUE, Service reservation
Office de Tourisme et des Congrès de Pau / AU064960001
Place Royale, 64 000 PAU, France
Tel : 00 33 5 59 27 17 49 - Fax : 00 33 5 59 27 66 63 - Mail : omt.service-groupe@pau.fr
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Office de Tourisme et des Congrès

Pau la vie rêvée des villes

SPECIFIC CONDITIONS GOVERNING HOTEL BOOKINGS
Booking service provided by the Pau Office de Tourisme et des Congrès

1 –Authorized Tourist offices (in accordance with the Law of 13th July 1992) may book and sell all types of leisure, accommodation and general services. They will assist participants by providing them a selection of hotels and booking rooms for the 24th AETE meeting.

2 – Bookings

- ***Accommodation and other services may be pre-booked before July 1st*** by the Office de Tourisme et des Congrès by returning the attached form by FAX or E-mail (omt.service-groupe@pau.fr).
Participants will then receive confirmation of room availability and the total cost of the reservation will be confirmed at this step (invoice).

- ***Bookings must be confirmed by post*** by sending the same booking form, together with full payment for hotel booking (credit card to be written on the form or bank transfer).
Your booking will be confirmed as soon as this last letter is received.

3 – Payment:

Payment may be made by debit or credit card (not American Express) or cheque, payable to the Trésor Public, or by bank transfer to the Banque de France - 64000 Pau:
Account number Bdf 30001_00622_C6410000000_87
From abroad: IBAN Code: FR76 1007 1640 00 00 0020 0042 876 / SWIFT Code: BDFEFRPPXXX
The total cost of the booking must be paid by July 31st otherwise the order will be cancelled.

4 – Documents issued:

A voucher will be sent back to participants to be exchanged against the booked service provision, along with your invoice.

5 – Participants wishing to cancel the booking, are invited to inform the booking service of the Tourist Office by telephone, fax or e-mail in order to inform individual hotels.
No charge will be asked for bookings cancelled up to 8 days prior to the start of the meeting.
If cancellation takes place within 8 days, 50% of the hotel fees will be charged.
No refund will be given in case of late cancelling without notification or if the stay is shortened without notification in due time. No charge will be applied for name changes.

6 – Claims/disputes

Any claim related to hotel bookings must be sent by registered letter to the Tourist Office, (the sole competent body to take a decision regarding any dispute within eight days of the end of the service provision). Any disputes arising from this payment or booking or contract options will be heard by the Pau administrative courts. Only the French text of this document may be taken into consideration. The accountant and signatory is the Trésorier Municipal de Pau, 4, rue Henri IV – 64000 PAU, the accounting representative of the Tourist Office, code number: 064026.

Françoise LAMARQUE, Service reservation
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