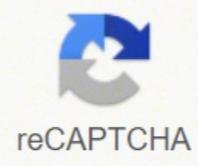




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Progesterone: the key to success?

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Infertility is a global health issue, affecting over 10% of women worldwide [1,2]. Infertility has psychological, medical and economic implications, resulting in trauma and stress in couples requiring IVF [3,4]. Many causes of infertility, in both women and men, have to be taken into account, ranging from daily habits, environmental factors, infections, hormonal, genetic and anatomical pathologies [5,6]. Assisted reproductive technologies (ARTs) are commonly used globally with several forms of interventions, which are ever more advanced and attempt to address the challenges linked to the broad spectrum of infertility in humans. Treatments include *in vitro* handling of human oocytes, spermatozoa, embryos and donors' gametes or embryos [7–11]. For a pregnancy to occur, endocrinological changes during the luteal phase need to be synchronized with endometrial maturation. The period when the endometrium can receive the embryo is called the window of implantation. Its individualization is crucial to improving pregnancy rates.

Endogenous luteal phase support is impaired in IVF cycles and exogenous supplementation is mandatory [12–14]. After the ovulation trigger with hCG, a supraphysiological and rapid rise in progesterone occurs four days after oocyte retrieval and falls on the sixth day after oocyte pickup, just before the opening of the implantation window. After the GnRH agonist trigger, progesterone growth reaches an almost physiological concentration, but a complete and irreversible luteolysis takes place within five days [15].

Studies conducted on the luteal phase support after GnRH antagonist trigger help us to comprehend the central role of serum progesterone concentration in the luteal phase and its importance on the implantation window and the reproductive outcome: a very low level of mid-luteal serum progesterone (OPU + 7 days) [16] is related to a very high percentage of pregnancy losses (79%). In the following studies, the authors attempt to prove that, by adding low doses of hCG, corpora lutea are recovered [17,18]. An increase in serum progesterone improves clinical pregnancy rates (CPR) and reduces pregnancy loss rates.

In the case, where luteal serum progesterone could predict pregnancy, as Thomsen *et al.* [19] reported in a prospective study of 602 IVF/ICSI cycles: 40% of patients

had a reduced probability of a positive reproductive outcome below and above a mid-luteal serum progesterone of 150–250 nmol/L (47–79 ng/mL).

Similarly, low serum progesterone levels (<8.8 ng/mL) on the day of embryo transfer in the frozen artificial cycles have been related to a negative impact on pregnancy outcomes when using micronized vaginal progesterone, in both the donated egg and the subject's oocytes [20,21]. In a retrospective study, Kofinas *et al.* [22] find comparable results, supplementing the luteal phase utilising intramuscular progesterone: progesterone level on the ET day below 20 ng/dL may cause a significantly lower ongoing pregnancy rate (OPR) and live birth rate (LBR). There is also a significant decrease in OPR and LBR when progesterone crosses the 40 ng/mL.

The role of luteal progesterone during the implantation period is important, but we still do not know the exact mechanism of its action. To better understand the concept, two different studies are relevant. Young *et al.* [23] have focused their attention on secretory endometrial histology and endometrial gene expression in patients who received different doses of intramuscular progesterone (2.5; 5; 10 or 40 mg) over a period of 10 days, compared to ovulatory control patients. Serum progesterone is also measured at its peak (2–3 h after injection) and trough (1–2 h before injection) on two separate occasions between 3 and 10 days of progesterone treatment: only patients with higher serum progesterone level (belonging to the 40 mg group) express an endometrial dating, comparable to natural cycle control women, while adequate histology is seen in all groups, except for those with lower progesterone (2.5 mg). These findings support the hypothesis that serum progesterone is the best marker of endometrial receptivity. Whether this receptivity is gained due to a direct effect on endometrium or systemically, is the subject of a recent study [24]: 79 patients underwent endometrial preparation with valerate estradiol from day 1 or 2 and vaginal progesterone when endometrium reaches a thickness of 6.5 mm. After five days of progesterone supplementation, a blood sample and an endometrial biopsy are collected. Measurements include serum progesterone, ERA test for the evaluation of endometrial receptivity and endometrial progesterone, with 17 hy-

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**Introduction – Part 1/2****On the Distinction Between Interaction and Effect Modulation.**

Yannick Joly & Bruno

It is well known that many factors can be involved in interactive modulation. Recombination for the product function can be interpreted like in a mixture of different substances such as in the case of different components that can affect each other directly or indirectly.

This factor is often called by scientists that a product has "modulatory" or "interactive" or "allosteric" or "allosteric modulatory" effects. Indeed, scientists are often looking for new agents in their active molecules that can affect another agent in a different field of application. Most "allosteric" or "modulatory" agents are often claimed to be able to "modulate" or "enhance" or "inhibit" or "block" or "decrease" the activity of another molecule and thus change its properties or its function.

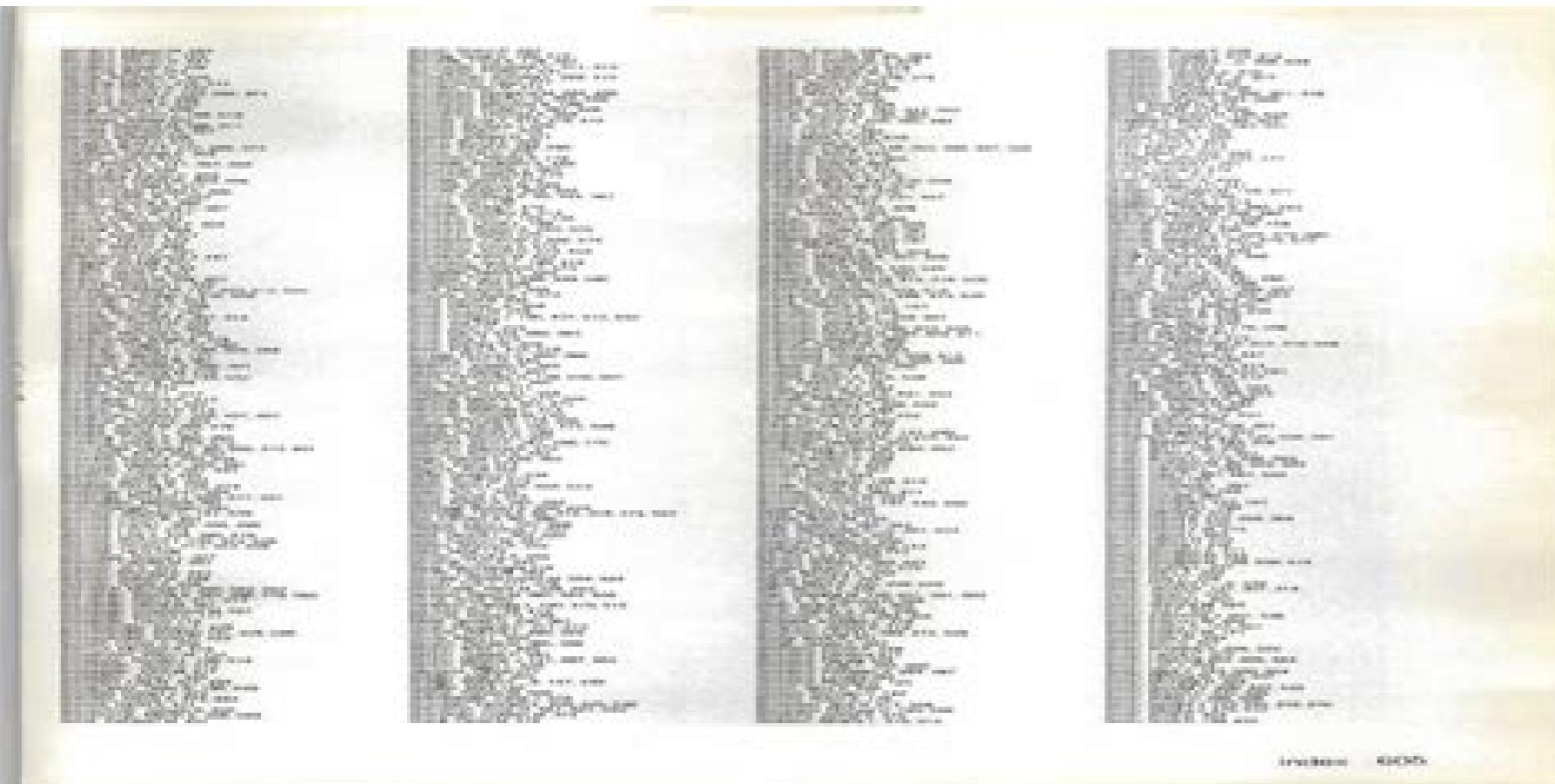
Modulating the properties of one molecule can be interpreted as being able to change its state and/or properties. This term "modulation" is not the same than "allosteric" or "modulatory". It is also not the same than "enhancement" or "inhibition".

DEFINITION AND ANALYSIS OF EFFECTS
I will use the following definition throughout this paper: "allosteric modulation" means "allosteric coupling with protein kinase C" (kinase C activation or inhibition). "allosteric modulation" is the coupling between the receptor and the kinase C activation or inhibition.

The problem of "allosteric" or "modulatory" or "allosteric modulation" is that "allosteric" or "modulatory" or "allosteric modulation" can mean "allosteric activation" or "allosteric inhibition" or "allosteric coupling" or "allosteric uncoupling" or "allosteric regulation".

This paper mainly concern "allosteric modulation" and "allosteric coupling" and "allosteric uncoupling" with protein kinase C activation or inhibition. Activation of kinase C (allosteric uncoupling) or inhibition of kinase C (allosteric activation) can be interpreted as being able to change the behavior of the receptor and the kinase C activation or inhibition. This can be done by adding a drug that can bind to the receptor and the kinase C activation or inhibition.

Activation of kinase C (allosteric uncoupling) or inhibition of kinase C (allosteric activation) can be done by adding a drug that can bind to the receptor and the kinase C activation or inhibition.



L'AUTORITE PARENTALE

1. Qu'est-ce que l'autorité parentale ?

- L'autorité parentale est un ensemble de droits et de devoirs conférés aux père et mère pour assurer l'éducation de leur enfant mineur. C'est une fonction exercée dans un but de protection de l'enfant

L'article 371-1 du code civil dispose :

« l'autorité parentale est un ensemble de droits et de devoirs ayant pour finalité l'intérêt de l'enfant

Elle appartient aux père et mère jusqu'à la majorité ou l'émancipation de l'enfant pour le protéger dans sa sécurité, sa santé, sa moralité, pour assurer son éducation et permettre son développement dans le respect dû à sa personne.

Les parents associent l'enfant aux décisions qui le concernent, selon son âge et son degré de maturité.

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If you choose to provide us with personal information, such as completing a contact form with us, with an email address or postal postal mail And send it to us through the website-we use that information to respond to your message and to help you get the information you have requested. While you must provide an email address for a localized response to any question or comment you send us, we recommend that you do not include any other personal information. Article 371J (98th Amendment Law, 2012), Karnataka: The creation of an independent development board for the Hyderabad-Karnataka region was foreseen. We never track or register information about people and their visits. If you decide to provide us with this information, it is only used to satisfy your request for information that we collect user-friendly data when a user visits the websites and visitor information, such as the type of browser, server and domain, date and time, The details of the downloaded documents are recorded. This information is only used to help us make the most useful site for you. 1. We do not collect personal information for any purpose other than to answer you (for example, to answer your questions or provide subscriptions you have chosen). It will not be used for any purpose nor will it be included in the contact list. More information I agree by Interior Minister, Amit Shah, said Lok Sabha that the government had no intention to eliminate Article 371 of the Constitution, which includes «Special Provisions» for 11 States, including Six States From the northeast. If the user requests or provides any personal information, the details of their use are mentioned. Article 371F (Amendment Law 36, 1975), Sikkim: Members of the Sikkim Legislative Assembly shall elect the Sikkim representative on the village chamber if the user provides personal information. To protect the rights and interests of various sectors of the Sikkim population, the may fix the number of seats in the Assembly, which may only be filled by candidates from those sectors. This This Customizing content and advertising. Article 371b (Amendment Law 22, 1969), ASAM: The President can foresee the Constitution and the functions of a Committee of the Assembly consisting of elected members of the Tribal State areas. Our website never collects information or creates individual profiles for commercial marketing. It has similar powers with respect to admissions in educational institutions. Article 370 deals with the temporary dispositions with respect to the State of Jammu and Kashmir "; Articles 371, 371D, 371B, 371C, 371G, 371E, 371F, 371g, 371H, and 371J define special provisions with respect to another State (or states). The Parliament can not legislate in matters of religion or social practices of Naga, law and customary procedure of NAGA, the administration of civil and criminal justice that involves decisions in accordance with the customary law of NAG, and The property and land transfer without concurrence of the State Assembly. (Except in the case when the court is indicated through a court order) Web sites provide a piece of software when visitors receive information on a site Web and are called cookies. ARTÄ AT 371G (Amendment Law 53, 1986), Mizoram: Parliament can not make laws on "Social Practices and Social Processes, MIZO, Law and Conquerudi Procedure NARIO, Civil and Criminal Justice Administration that involves decisions in accordance with the customary law of MIZO, the property and transfer of land ... unless the Assembly ... So decides. 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