

RODIFertility®

Conceive Your Dream



RODINK™

Your premium formulation specifically designed for use during pregnancy



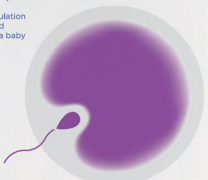
During Pregnancy

With fatty acids and Vitamin D that contributes to the normal function of the immune system

Patent Pending Technology

RODINKplus™

Your premium formulation specifically designed for when trying for a baby



Before Pregnancy

With fatty acids and Vitamin D that contributes to the normal function of the immune system

Patent Pending Technology

RODIOVA™

Your premium choice while trying for a baby



Before Pregnancy

With vitamin B6 that contributes to the regulation of the hormonal activity

RODIVITA™

Your premium choice when trying for a baby



Before Pregnancy

With fatty acids that contributes to the maternal tissue growth during pregnancy

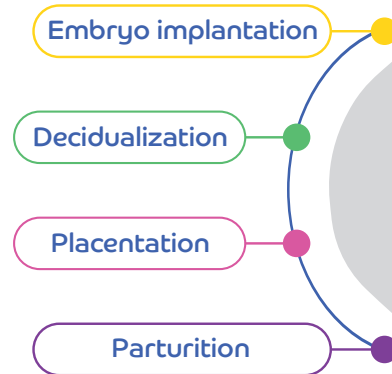
Slow Release Technology



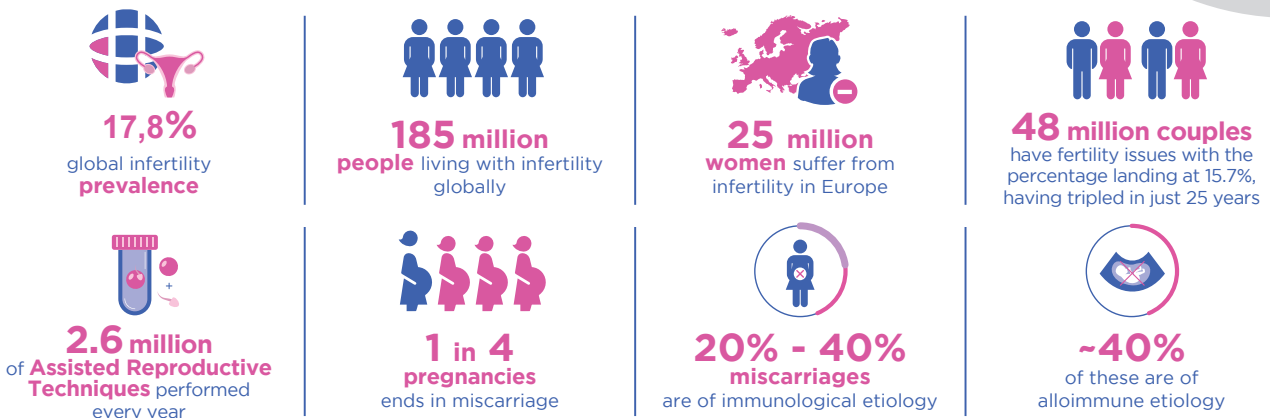
HUMAN REPRODUCTION AND PREGNANCY

Pregnancy is a unique type of immunological process and a well-choreographed physiological process that involves dynamic maternal and fetal dialogue being reliant on the success of a series of critical inflammatory events.

Although there are major advances in genetics, immunology, and endocrinology infertility reached a worldwide 15% prevalence.



INFERTILITY IN NUMBERS^{1,2,3,4}



IMMUNE-MEDIATED infertility rises as research advances

Today



Today we have a better understanding of what relates to infertility and miscarriages.

Several specific causes previously 'Unknown' have been identified, with the immune-mediated ones to rank on the top of this list's importance.

Autoimmune-mediated Alloimmune-mediated

IMPLANTATION FAILURES AND MISCARRIAGES is still a frustrating clinical problem



Recurrent or repeated implantation failures (RIF) and recurrent spontaneous abortions (RSA) may emerge during different phases in the embryo's journey and may be attributed to shared molecular factors and pathways.

Women diagnosed with RIF or RM experience numerous futile IVF attempts along with psychological distress and financial burden.

Early prognosis markers could be of added value, enabling optimal management and efficient therapeutic approaches.

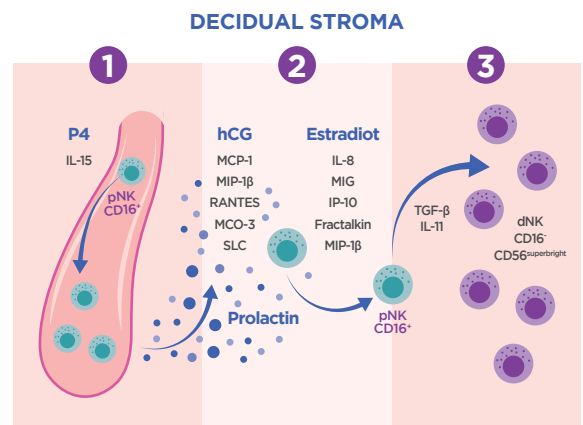
NK CELLS AND THEIR PIVOTAL ROLE IN PREGNANCY

Natural Killer (NK) cells in immune-mediated implantation failure and pregnancy loss

Women diagnosed with RIF or RM experience numerous futile IVF attempts along with psychological burden.

Decidual NK (dNK) cells constitute ~60–90% of immune cells in the decidua during implantation and in first trimester of pregnancy and play a major role in influencing adaptive immune responses and immune regulation.

They derive from peripheral blood NK cells (pNK), which have the phenotype CD3⁺ CD16⁺ CD56⁺ and are characterized by cytotoxic activity and the production of Th1 cytokines. Under the influence of hormones and cytokines, pNK multiply and are selectively recruited into the implantation site by chemotactic agents produced by the trophoblast, the endothelium and decidual epithelium. In the endometrial environment, under the influence of growth factors and cytokines, pNK cells differentiate into CD3⁺ CD16⁺ CD56^{bright} cells with low cytotoxic activity (dNK).⁵



Adapted from Olmos-Ortiz A et al.⁵

Peripheral NK cell: a predictor of RIFs and miscarriages

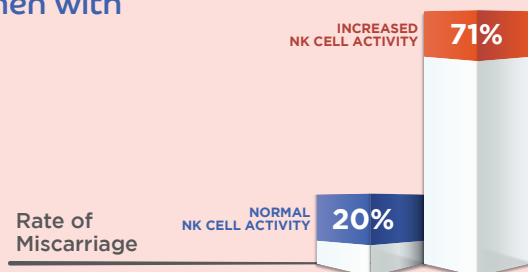
Focusing on the increase of pNK cells has been reported as one of the most frequent immunological findings in women with implantation failures (16% in RIF women).⁶

In practice, peripheral blood immunophenotyping for the detection of NK cell disturbances is routinely used for the identification of women with alloimmune etiology for their subfertility.⁷

Higher Probability for a miscarriage in women with High NK Activity⁸

Elevated NK activity had a positive predictive value of 71% for a subsequent miscarriage in recurrent-miscarriage patients, as compared with 20% in women with a low NK activity.

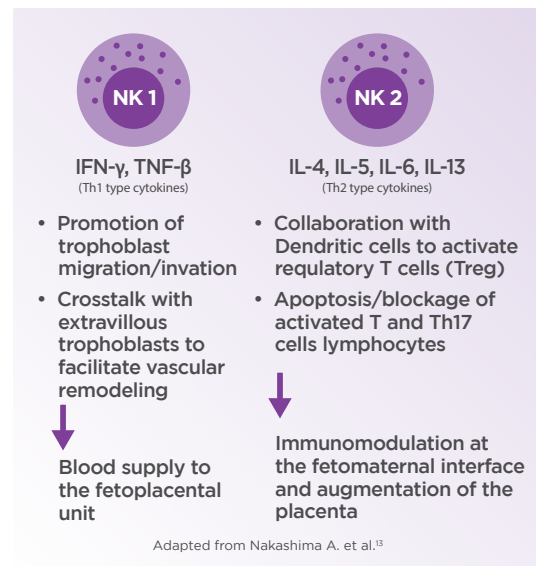
pNK cell numbers of <12% were strongly associated with a subsequent pregnancy carried to term.^{9,10}



Decidual NK cells

dNK cells bear a heterocladic repertoire of inhibitory and activating receptors through which they recognize selected epitopes on HLA class I molecules (HLA-G, E, C) expressed on invading trophoblast.⁶ High affinity interactions of NK receptors with their ligands provide self-signals to either cytotoxic dNK activation (Th1 response) or inhibition of activation and protection of the trophoblast (Th2 response) (“NK cell allorecognition system”).¹¹

Depending on different signals exchanged between the endometrium and the blastocyst, dNK cells can function as regulatory, cytotoxic, tolerant or memory cells. The distinction of dNK to different functional subpopulations give them a multilateral role in pregnancy: trophoblast invasion, decidualization during implantation, immunomodulation and augmentation of the placenta during gestation.¹²



Adapted from Nakashima A. et al.¹³

NK cells and their Pivotal role in RSAs and RIFs

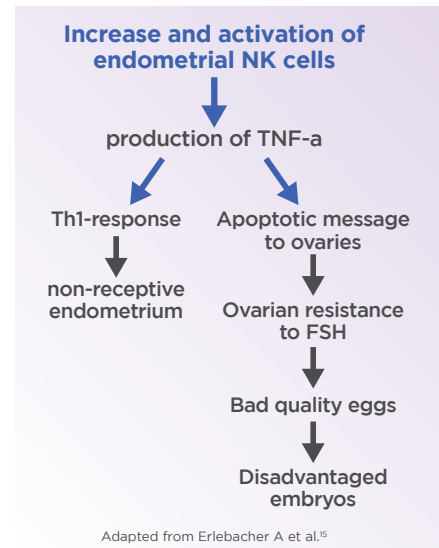
A significant percentage of unexplained RSA is due to rejection-type reactions of the pregnant women against the semi-allogeneic fetus. The disruption of one or more of the mechanisms leading to tolerance in normal pregnancy may lead to miscarriage.

The central mechanism of the embryo “rejection”

The predominance of a Th1 cytotoxic response or defective production of Th2-type cytokines.

RSAs: Repeated Spontaneous Abortions

In response to the conceptus or other antigens, decidual lymphocytes secrete Th1-type cytokines (IL-2, IFN- γ , TNF- α), which adversely affect the development of the embryo with the production of pro-inflammatory cytokines (i.e. IL-6) resulting in insufficient regulation of inflammatory immune responses incompatible with successful pregnancy. The regulatory CD4⁺CD25^{bright} T lymphocytes (Treg), which normally inhibit the proliferation of autologous CD4⁺ T cells, are reduced to the benefit of Th17 cells and the production of pro-inflammatory cytokines (i.e. IL-6) resulting in insufficient regulation of inflammatory immune responses incompatible with successful pregnancy. In the context of the Th1-type response, dNK cells become activated (NK1 phenotype) and may damage the trophoblast either by direct cytotoxicity or by the secretion of proinflammatory cytokines constituting the main cytotoxic cell population involved in cases where the embryo is “rejected” by the mother.¹⁴



CD56⁺ CELLS

An indicator of both high specificity and high positive predictive value in pregnancy loss

A longitudinal study revealed that RSA women compared to controls, had higher numbers of CD56⁺/16⁺ and increased NK cell cytotoxicity during early pregnancy.¹⁶ A prospective study in 114 pregnant women demonstrated that, elevated CD56⁺ cells in pregnant women (who are not donor egg recipients, or who have not undergone an ICSI procedure, and not carrying multiple gestation) predicts loss of a karyotypically normal conceptus with a **specificity of 87%** and **positive predictive value of 78%**.¹⁷

Down regulation of NK cells in women with RSA is associated with a favorable pregnancy outcome.^{18,19}

The percentages of **CD56⁺** and **CD56⁺/16⁺ cells** in the peripheral blood on the day of embryo transfer were significantly higher in women with IVF failure than in women with successful implantation.²⁰

RIFs: Repeated Implantation failures

Endometrial CD3⁻CD16⁻CD56^{bright} NK cells may be activated in response to infection or to potentially transformed or over invasive trophoblasts, and produce TNF- α which induces Th1 response associated with non-receptive endometrium and can also release message for ovarian apoptosis associated with poor ovarian response to endogenous and exogenous FSH and ultimately low egg quality and dyspragic embryos.

EXISTING LITERATURE REVIEW

Although NK changes in cases of miscarriages take place at the maternal-fetal interface, it is for long accepted that the disturbances are also reflected in women's peripheral blood.²¹

Conventional CD3⁻CD56⁺CD16⁺ NK cells are increased in the uterus (abortion material) but also in the blood of women at the time of abortion.²¹

Meta-analyses confirm the increase of pNK cell numbers or percentages in RSA women, but NOT the increase of uterine NK cells or a significant correlation between pNK and dNK.²²

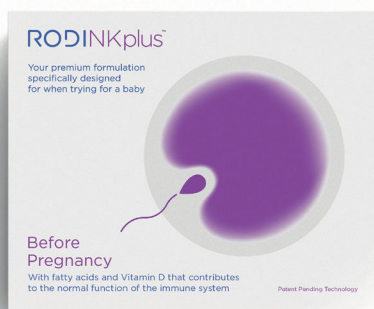
RODI Fertility® Portfolio

& IMMUNE EQUILIBRIUM

Based on 7 years of intense research on reproductive medicine with a focus on conception and successful pregnancy outcomes, **RODI Fertility** has developed a comprehensive line of products for use before and during pregnancy with **first-of-a-kind** patented technology in all major markets worldwide including U.S.A., Europe, Japan, India, Russia and Southeast Asia.

RODINKplus™

award-winning clinical study ✓

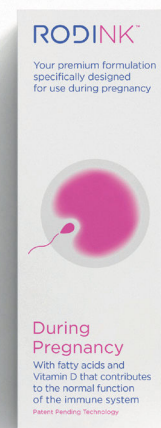


Oral administration
1 vial a day
in the morning

Recommended duration of use
40 consecutive days before trying to conceive



RODINK™



Oral administration
10 ml once a day
in the morning

Recommended duration of use in the first 3 months of pregnancy

BEFORE PREGNANCY

Backed by an awarded clinical study, **RODI NK plus™** contains 40 rare-to-find fatty acids and vitamin D3, with its combination altogether contributing to the equilibrium of a potentially aggressive immune system function in the period before pregnancy.



DURING 1st TRIMESTER OF PREGNANCY

RODI NK™ is a key ally for immune equilibrium while expecting a baby. Its patented technology is specifically formulated to continue supporting women during the first three months of pregnancy contributing to the normal function of the immune system.

WHAT MAKES RODI NK PLUS & RODI NK

RODI NK plus™ and **RODI NK™** are not an omega 3 fatty acids combination products, but highly sophisticated formulations designed by a panel of experts and studied in the fertility context.

Some of the formula's fatty acids include miristic acid, palmitic acid, oleic acid, LA: linoleic acid, ALA: a-linoleic acid, GLA: γ-linoleic acid, behenic acid, erucic acid, lignoceric acid, gondoic acid and more, ~~omega 6 & 7~~ in forms of mono-glycerides, di-glycerides, tri-glycerides and esters thereof, plus vitamin D3 and antioxidants.

WHAT RESEARCH DEMONSTRATES IN HOW OUR INGREDIENTS CONNECT WITH FERTILITY

FATTY ACIDS

Research indicates the existence of several novel mechanisms by which altered fatty acid availability can modulate immune responses and impact upon clinical outcomes, including those associated with T cell responses, antigen presentation and fatty acid-derived inflammatory mediator production

TOCOPHEROLS (Vitamin E)

Act as an antioxidant and can be found in the fluid around developing eggs.

- Help prevent recurrent miscarriages
- Support a healthy amniotic sac in pregnancy
- Prevent the premature rupture of the membranes in pregnancy

The tocopherols used in **RODI NK plus™** formulation are 100% natural and protect the product's formulation against oxidation.

VITAMIN D3

Has a pivotal role in regulating immune responses and has immune regulatory effects on NK cell cytotoxicity in women with recurrent pregnancy losses. Vitamin D deficiency may be a risk factor for recurrent pregnancy losses by increasing cellular immunity and autoimmunity. Vitamin D is involved in regulation of both NK cell population and cytotoxicity.²³



• PUBLISHED STUDY²⁴

INHIBITORY EFFECT OF A FATTY-ACID-BASED ORAL FORMULA ON PERIPHERAL BLOOD NK CELLS OF SUBFERTILE WOMEN.



RODI NK plus GROUP
42 WOMEN
(ages 22-49)



CONTROL GROUP
50 WOMEN
(ages 22-49)



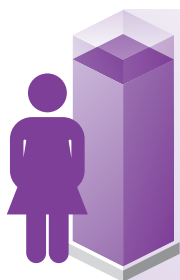
**40 DAYS
DURATION**



**EXPERIENCING
RIF AND RSA**

The 42 women experiencing RIF and/or RSA who had elevated levels of peripheral NK cells in multiple testings, were advised to use a daily dose of **RODI NK plus** for **40 consecutive days**. The levels and cytotoxicity of NK cells were evaluated in two consecutive measurements before and after the use of **RODI NK plus**.

NUMBER OF NK CELLS BEFORE AND AFTER USE OF RODI NK plus



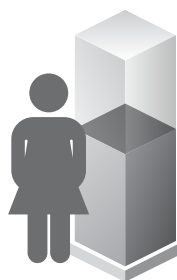
RODI NK plus Group

**88.1%
of women (37/42)**

had a decrease in the pNK cells percentages (P value: <0,0001)

mean value of PB NK cells %
before: 19,5±7,36 %
after: 15,24±5,05 %

80.1% decrease



Control Group

**54%
of women (27/50)**

had a decrease in the pNK cell percentages (P value: <0,728)

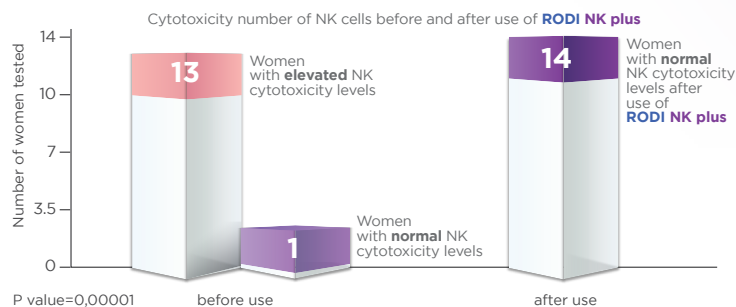
mean value of PB NK cells %
first measurement: 18,22±5,44 %
second measurement: 17,92±6,35 %

46% decrease

NK cytotoxicity

was normalized in all group

after the **40 days of using RODI NK plus**, although initially found increased in 13 out of 14 women



• AWARD-WINNING CLINICAL STUDY²⁵

Scientific research award at Panhellenic Congress of Autoimmune Diseases, Rheumatology and Clinical Immunology (2019)



EFFECT OF A PATENTED FATTY ACID-BASED ORAL FORMULA ON PERSISTENTLY HIGH BLOOD NK CELL LEVELS OF INFERTILITY WOMEN EXPERIENCING REPEATED REPRODUCTION FAILURES.



RODI NK plus GROUP
26 WOMEN
(ages 22-49)

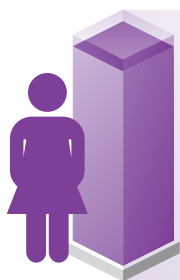


**40 DAYS
DURATION**



**EXPERIENCING RIF AND RSA
AND NK CELLS >18%**

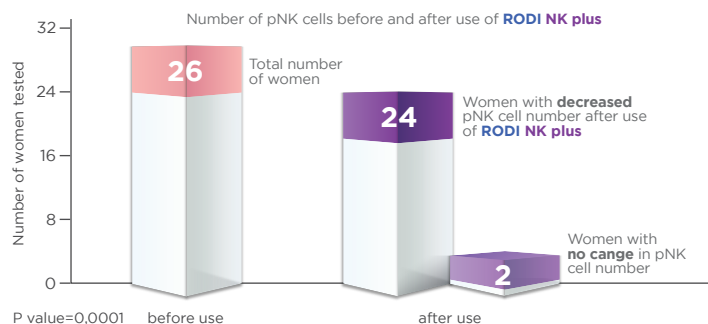
The 26 women experiencing **RIF** and/or **RSA**, had **persistently high** blood NK cell levels (>18%) and were advised to use a daily dose of **RODI NK plus** for 40 consecutive days. The levels of NK cells were measured before and after the use of **RODI NK plus**.



RODI NK plus Group

**92.3%
of women (24/26)**

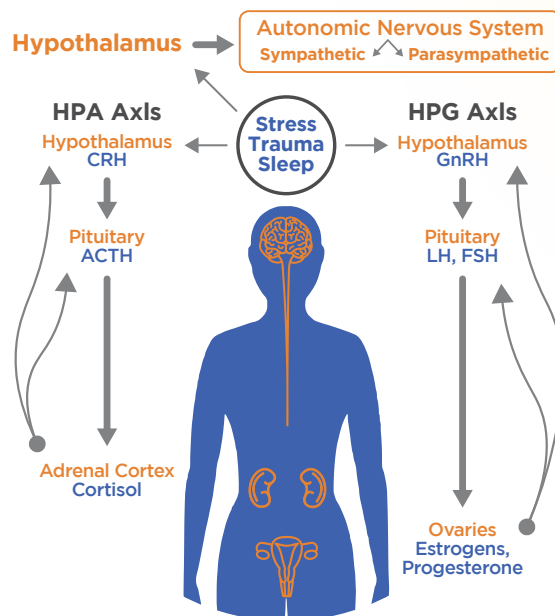
had a 30% decrease in the pNK cell percentage



THE ROLE OF HPG AND HPA AXIS

The **hypothalamic-pituitary-gonadal (HPG) axis** is primarily responsible for regulating reproductive activity and the release of ovarian hormones.²⁶

The HPA axis is responsible for **the neuroendocrine adaptation component of the stress response**. This response is characterized by hypothalamic release of corticotropin-releasing factor (CRF) also known as CRH or corticotropin-releasing hormone.



One of the most important functions of the **HPG axis** is to regulate reproduction by influencing the ovarian and uterine cycles. Over years, HPG axis activity decreases and women cease to be fertile. Keeping the HPG axis balanced is important since it significantly affects various physiological processes.

RODI OVA™ is designed by doctors and is based on international scientific research, providing an optimum selection and dosage of nutrients while your body works on delivering its eggs. The carefully selected ingredients for **Day and Night intake** are designed to best fit a full day's activities.

Myo-inositol & HPG axis

Myo-inositol plays a key role in fertility, as it participates in the signaling cascade of the **HPG axis** and is the second messenger of the FSH and LH.

In fact, myo-ins is the second messenger of the follicle stimulating hormone (FSH) and luteinizing hormone (LH), involving a long-way transduction cascade from the pituitary gland to other body districts.^{27,28}

FSH correct signaling allows the maturation of follicles and regulates the selection of the dominant follicle. Such processes also depend on insulin signaling, which is also mediated by myo-inositol.

RODIOVA
Your premium choice while trying for a baby

Before Pregnancy
With vitamin B6 that contributes to the regulation of the hormonal activity

lemon flavour

Oral administration
2 times a day in the morning and at night

Recommended to take
for 3 months before trying for a baby

BEFORE PREGNANCY

Melatonin & HPA axis

Melatonin can effectively activate the protective signal pathway in nerve cells and exert an antidepressant role.

The **HPA axis** is an integral part of the neuroendocrine system, which regulates the body's ability to respond to stress. In turn, sleep loss influences the HPA axis, leading to hyperactivation.

Studies have demonstrated that melatonin improves oocyte quality, increases fertilization rates and reduces oxidative damage in the follicular fluid.²⁹

hormonal balance

IT'S ALL ABOUT THE EGG

Because of these activities in the gonadotropin and the insulin pathways, several authors investigated the efficiency of myo-ins administration in achieving pregnancy in infertile PCOS and non-PCOS women, either for natural conception or during assisted reproductive technology (ART) protocols.

MYOINOSITOL AND MELATONIN IN THE PURSUIT OF PREGNANCY

The correct signaling of FSH allows the maturation of follicles and regulates the selection of the dominant follicle.³⁰ Such processes also depend on insulin signaling, which is also mediated by myo-ins.

Inositol in Gonadotropin Signaling

During a physiological menstrual cycle, signals from the hypothalamus-pituitary-gonadal (HPG) axis promote the progression of folliculogenesis through the stimuli of follicle stimulating hormone (FSH) and luteinizing hormone (LH) whose synergistic activity regulates gonadal functions. Myo-ins participates in both signaling pathways of FSH and LH. The inositol phosphate production is triggered only by elevated FSH levels, indicating the importance of inositol immediately before and during ovulation.²⁷

Inositol in Insulin Signaling

The correct signaling of FSH allows the maturation of follicles and regulates the selection of the dominant follicle.³¹ Such processes also depend on insulin signaling, which is also mediated by myo-ins. Studies have shown that myo-ins supplementation can reduce systemic levels of insulin in cases of hyperinsulinemia, which inhibits the progression of the menstrual cycle that reduces fertility.

Myo-ins could prevent the onset of neural tube defects and the occurrence of gestational diabetes mellitus, promoting a trouble-free gestation. Due to the safety and efficiency of myo-ins, such a treatment may also substitute several pharmaceuticals, which are contraindicated in pregnancy.³⁰

Keeping the HPG Axis Regulating Normally

Melatonin may directly affect ovarian function. It is concentrated in human ovarian FF relative to the level in plasma, and melatonin alters granulosa cell (GC) steroidogenesis and follicular function in humans.

Both regular circadian rhythms and cyclic melatonin availability are beneficial in assuring optimal reproductive physiology in females. For successful ovulation, regular cyclic events at the hypothalamopituitary level ensures properly timed gonadotropin release which leads to extrusion of the mature oocyte from the ruptured graafian follicle.²⁹

Melatonin is synthesized in the peripheral reproductive organs, including granulosa cells, the cumulus oophorus, and the oocyte and from these sources and the blood probably assist in the maturation of the oocyte and protect it from free radical damage, especially at ovulation. It is a powerful free radical scavenger and protects the oocyte from oxidative stress, especially at the time of ovulation.³²

Melatonin produced in the placenta may preserve the optimal function of this organ.

Melatonin could become an important medication for improving ovarian function and oocyte quality, and open new opportunities for the management of several ovarian diseases.

RODIVITA™

becoming healthy before
becoming pregnant

Pre-conception nutrition is a vital part of preparing for pregnancy. Factors such as BMI and what a woman eats, can play an important role in health during pregnancy and the health of your developing fetus. For many women it may be hard to steadily follow a well-balanced diet before pregnancy and may not have the proper nutritional status for the demands of pregnancy, so adding a proper multivitamin nutraceutical is recommended.

RODI VITA™ completes the **RODI Fertility®** portfolio bringing a sophisticated product design that is based on international scientific research, aiming to help you provide your body with an optimum selection and dosage of essential prenatal vitamins and minerals during the period before trying for a baby.

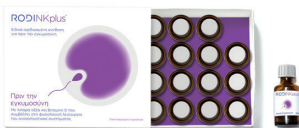


Myo-inositol, Choline, Folic acid, Biotin, Vitamin-E, Vitamin D3, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B12, Vitamin B6, Iron, Selenium, Melaonin

RODINKplus™

IMMUNE EQUILIBRIUM BEFORE PREGNANCY

The clinically backed patented technology with fatty acids and vitamin D3 which contributes to the normal function of the immune system when trying for a baby.



RODINK™

IMMUNE EQUILIBRIUM DURING PREGNANCY

The patented technology with fatty acids and vitamin D3 which contributes to the normal function of the immune system during the first three months of pregnancy.



RODIOVA™

IT'S ALL ABOUT THE EGG BEFORE PREGNANCY

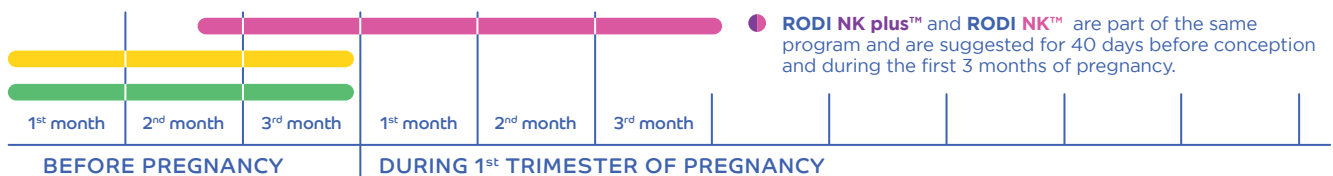
A premium formulation with vitamin B6 which contributes to the regulation of the hormonal activity before pregnancy.



RODIVITA™

A SUPREME PRENATAL MULTIVITAMIN BEFORE PREGNANCY

An essential prenatal nutraceutical based on vitamins, minerals and amino-acids in doses scientifically determined according to the body's needs for a successful pregnancy.



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“SUPPORTING WOMEN
THROUGH THEIR JOURNEY TOWARDS
MOTHERHOOD”



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