Downstream product market research of Melatonin	
Product name and physical & chemical properties	Melatonin (N-acetyl-5-methoxytryptamine), also known as pinealin, is a class of steroid hormones secreted by mammals and human pineal gland. It has also been reported that mammalian retinas and accessory lacrimal glands also produce small amounts of melatonin; some warming animals can also synthesize melatonin in the eyes, brain and skin (such as frogs) and certain algae.
Product Usage	Melatonin has the functions of sedative hypnosis and regulation of sleep awakening cycle, regulation of endocrine system, maintenance of internal environment stability, enhancement of immunity, and delay of aging. In the regulation of melatonin in many aspects, its regulation of sleep is prominent, and it has obvious therapeutic effects on sleep disorders caused by sleep delay syndrome and abnormal time difference.
Product principle / mechanism	The secretion of melatonin is related to light, and it is circadian rhythm. Daytime light information can be transmitted to the suprachiasmatic nucleus through the retina and optic nerve to inhibit melatonin secretions, and nighttime melatonin secretion is increased. In addition, melatonin secretion The level is also related to age. After 35 years old, gland function is reduced, melatonin secretion is reduced, and the average per 10 years is reduced by 10% to 15%. However, the amount of melatonin secretion in elderly sleep disorders is more obvious, only the peak. One tenth of the period. People with primary insomnia or irregular day and night life, people with frequent jet lag have abnormalities in melatonin secretion. The melatonin level can be maintained in a normal state by supplementing melatonin, which is used to adjust sleep, increase deep sleep time, improve sleep quality, and has an effective rate of about 95%, no side effects of anti-stable drugs, no addiction.

What is the relationship with the project / how to use the results of the project	The biological clock is an intrinsic mechanism that adapts to the cyclical changes of environmental factors such as light and temperature. As an intrinsic mechanism to adapt to the environment, the biological clock plays an important role in regulating metabolism. Many hormones that regulate important metabolic pathways are regulated by the circadian clock. These hormones such as insulin, glucagon, adiponectin, and leptin can transmit central nervous system information to tissues and organs that are responsible for metabolism in the periphery. Steady state is very important. Many important metabolic pathways, such as blood glucose and amino acid metabolism pathways, are also regulated by the circadian clock and have significant circadian rhythms. However, some special occupations, such as flight attendants, cruise ship soldiers, etc., need to travel in different time zones every day, or often travel across countries, staying up late, and so on. The clock is often disrupted, even without a prescribed biological clock. The people are fighting the jet lag almost every moment. The time difference makes the living routine that people build up for a long time is broken, and the nerve medium still secretes and regulates metabolism according to the original time period, which causes the body to feel uncomfortable. It usually manifests as drowsiness, fatigue, inattention, short-term memory difficulties, poor abstract cognitive ability, irritability, slow thinking, and reduced work efficiency. The severity of this disorder is directly proportional to the number of hours of the time difference. When the time difference exceeds 4 time zones, there will be a significant reaction, such as sleep disorders and decreased alertness. In addition to dietary adjustments, psychological cues, and early adjustments to sleep patterns, a class of drugs represented by melatonin also has a place in the field of “how to scientifically reduce jet lag”. Therefore, we can produce melatonin by using E. coli which has successfully constructed the KaiABC system and has circadian rhythm in the cell.

The company that currently produces the product on the market	America： GNC; ON; Vitafusion Sleep Well; Natrol Melatonin Australia：Swisse sleep; China：Centrum; TRT; Natrol melatonin
Consumer feedback	1. Overall, melatonin is positive in treating insomnia, but it is weak. A 2005 review of 15 placebo-controlled studies found that melatonin reduced sleep time by an average of 3.9 minutes compared with placebo, and sleep duration increased by 13.7 minutes. Sleep efficiency (actual sleep in lying The proportion of bed time) increased by 3.1%. In contrast, the common prescription sleeping pills, benzodiazepines, on average, can speed up sleep for about 10 minutes. In 2011, the European Food Safety Authority conducted a review of the evidence for melatonin and concluded that "melatonin can help reduce the time it takes to fall asleep." Patty Deuster is the author of a melatonin system review in 2014. Her team pooled 35 randomized, placebo-controlled studies in healthy individuals with or without diagnosis of insomnia. Dusit said that melatonin is positive for insomnia, but it is "weak" and requires more large-scale studies. Her retrospective analysis found that melatonin has a weaker effect in helping to fall asleep, stay asleep and have a jet lag. And it can not conclude the effect of shifting and adjusting the biological clock. 2. However, melatonin may be especially helpful when a person is troubled by jet lag. Because it can help people adjust the biological clock, it can also promote sleep after a long flight. In 2002, the Cochrane Library of the Evidence-Based Medicine Database evaluated the effects of melatonin on jet lag. The conclusion is that "melatonin is quite effective in preventing and reducing jet lag, and occasionally short-term use seems safe." "Eight of the ten trials found that taking melatonin at the bedtime of the destination reduced the jet lag after a flight that spanned five or more time zones."

Research sentiment/feasibility analysis	1. side effect Regarding the side effects of using melatonin, some researchers reviewed the adverse reaction reports in 35 studies, and found no serious problems. The most frequently reported side effects are lethargy (in a sense, this is also what people want) and headaches. However, some researchers have indicated that melatonin may have adverse effects in some cases. For example, for some people with specific genetic variations, melatonin can impair the body's ability to handle blood sugar. In addition, there is a lack of corresponding assessment of the risks of prolonged use. There is currently no clear study evaluating the use of melatonin for more than 6 months. 2. usage time Researchers have not systematically evaluated when melatonin should be used. Professionals have not reached a consensus on this – it depends on whether they think melatonin is better at promoting sleep, or better at adjusting the clock. According to some researchers, the ability of melatonin to regulate circadian rhythms is stronger than that of immediate promotion of sleep. Therefore, these people believe that users should take it a few hours before going to bed, rather than when they are going to sleep, which can "advance" the clock for about half an hour. It is also believed that taking melatonin in the afternoon or evening can most effectively advance the circadian clock phase, which means that the user's circadian clock will become earlier on the next day. According to this theory, it is also helpful to receive sunshine in the morning, even more effective than melatonin. However, other researchers do not recommend taking melatonin several hours before bedtime. He believes that the ability of melatonin to instantly promote sleep (though weak) means that people should take it before going to bed. In general, the ideal time for an individual to take melatonin is difficult to predict. Melatonin is "not easy for consumers," and many health practitioners may not know the subtleties. 3. Dosage and vigilance At present, the production and use management of melatonin is quite confusing. Most of the melatonin that

	can be found in the market has no drug production license and no approval for the drug substance. Secondly, as a hormone, it should be dose-limited. However, melatonin does not currently have a safe dosage standard. At the pharmacy, it is easy to find 10 mg of melatonin per tablet, but this dose may be too much. Many studies have found that melatonin can achieve similar effects at high doses at low doses (1 mg or less). Moreover, too high a dose may make your brain less sensitive to this hormone. So, if you really want to use it, start with a small dose and see if it works.