

2251 Dick George Rd., Cave Junction, OR 97523



# We are working to bring advanced technology for diagnostic and preventive medicine to the American people.

# Medical Break-through at the Oregon Institute of Science and Medicine

Scientists at the Oregon Institute of Science and Medicine, a nonprofit research institute, have been working to improve diagnostic, therapeutic, and preventive medicine. Now, they have made a remarkable break-through.

As reported in the Fall 2017 issue of the *Journal of Ameri*can Physicians and Surgeons, they have discovered metabolic patterns that are predictive of heart attacks and breast cancer by means of analysis of a tiny drop of urine – *before* symptoms arise and *before* medical diagnosis takes place.

As we live, our bodies produce thousands of different chemicals required for life and many that are discarded as by-products. These compounds – which make their way into our urine, blood, breath, saliva, and other tissues – contain a wealth of information about our current and future health. Urine contains the most information at the lowest cost.

Consider the scourge of breast cancer. This disease develops slowly and eventu-



symptoms. It is of great importance to detect breast cancer early in this process, take steps to prevent it, and – if it occurs – to monitor it very carefully during medical therapy.

It is best to detect breast cancer so early that the increased probability of the disease can be fought therapeutically by less invasive means, rather than waiting until disease symptoms arrive and require severe, less effective treatment.

OISM scientists have found metabolic patterns in human urine that are *predictive* of developing breast cancer – measurable *before* symptoms are present. This opens the way toward true preventive actions against this dangerous disease.

More remarkably, OISM scientists have now found metabolic patterns in human urine that are *predictive* of heart attacks – measurable *before* symptoms are present, even in well people with no history of heart disease.

About 25% of Americans in middle age and older die from heart disease. Many of these deaths occur entirely without warning by a sudden heart attack. Yet, modern medical procedures can save many of these lives – *if* there is warning before the heart attack.

Moreover, this method of predicting heart attacks and cancer, when fully developed and automated, could be offered to ordinary people at a cost of \$10 or less, without costly medical visits, by merely mailing a drop of dried urine to a central laboratory and receiving a report by Internet.

If developing disease is found, then preventive and therapeutic intervention can take place – to fight the probability of illness rather than illness itself.

These discoveries can save many lives and prevent much suffering, *and the same analysis*, with further research, will simultaneously predict most other degenerative diseases and many other conditions.

This figure illustrates the goal of this work. The red line is the current lifespan of Americans. The blue line is the objective. Everyone should have an opportunity to live a full length human life, without early suffering and death.

Now, technology is within reach of this goal.

<u>We need your help</u> as a volunteer urine donor in order to extend development of analytical procedures that can revolutionize the evaluation of personal biochemistry – and thereby improve the health, happiness and prosperity of everyone, including their children.

#### **Metabolic Profiling**

The research field called "metabolic profiling" began in 1968 with a hypothesis originated by Art Robinson, then on the faculty of the University of California at San Diego.

During the following 10 years, Art, Linus Pauling, and a dozen scientists and engineers, from Caltech, UCSD, Stanford, and the Linus Pauling Institute of Science and Medicine, worked to test and eventually prove this hypothesis, showing that this could be very useful in diagnostic medicine.

With the best technology available in the 1970s, they were able to measure about 100 metabolic urinary compounds by analytical methods that required 6 hours. They also studied



the components of breath and other tissues.

This picture shows Art's scientist wife Laurelee calculating disease patterns in these metabolic profiles. The thin lightcolored object on the right side of Laurelee's computer was the most advanced minicomputer disk storage drive at Stanford University when they acquired it. It cost \$20,000 in 1972 and had a capacity of one megabyte, Mb.

In the 1970s, they found unique profiles for overt breast cancer, multiple sclerosis, muscular dystrophy, Huntington's disease, degenerative aging, and other conditions.

While confirming Art's hypothesis, this work had three weaknesses. First, the analytical technology was slow and expensive. Second, the work was done on samples from people who were already ill. Third, they measured single samples from individual people, rather than multiple samples over a period of time, which could personalize the technique.

Scientists at other institutions entered this field that Art originated, but their work, too, had these impractical disadvantages. Metabolic profiling was ahead of its time.

In 1981, Art and Laurelee, with the help of several colleagues, including Martin Kamen, discoverer of carbon 14 and much of the tracer methodology used in biochemistry, and Nobel Prize winner Bruce Merrifield, discoverer of synthetic methods that underlie modern protein and DNA chemistry, founded the Oregon Institute of Science and Medicine, near Cave Junction, Oregon.

Early research at OISM involved primarily nutrition and cancer and protein chemistry. Unfortunately, metabolic profiling had to wait until more advanced analytical technology was developed. While other medical technology has advanced, it is mostly far too expensive for use in preventive medicine and is used largely by physicians for already ill people. Metabolic profiling is potentially much better.

Art will never forget his wife Laurelee's last words before she went to sleep for the last time. She had a stomach ache. He asked her if she wanted to go to the emergency room. That room, however, was a long drive away for a sick woman in the middle of the night. She said she preferred to wait until morning. She had seen doctors twice, but they had not ordered the expensive clinical tests she actually needed.

Morning, for her, never came. She died that night at age 43 from a rare pancreatic disease that could have been detected much earlier and treated successfully – detected by the metabolic profiling analytical techniques that had been, in addition to her children, her life's work for more than 15 years.

When Laurelee died, her children were Zachary, Noah, Arynne, Joshua, Bethany, and Matthew, ages 12, 10, 8, 6, 6, and 1 years, respectively. Today, all six have advanced degrees in science, engineering, or medicine, and five still work with their father and their colleagues at OISM.

Millions of such stories could be told about the unnecessary deaths that have occurred since that time. It is time to bring inexpensive diagnostic technology to ordinary people.

It is time to stop these deaths.

### **Current Metabolic Profiling**

The discovery of metabolic profiles present before symptoms of disease for heart attacks and cancer (published in Noah Robinson, Matthew Robinson, and Art Robinson, "Metabolic Profiling with Magnetic Resonance Mass Spectrometry and a Human Urine Bank: Profiles for Aging, Sex, Heart Disease, Breast Cancer, and Prostate Cancer," *Journal* of American Physicians and Surgeons 22, 3 (2017) pp 75-84) was made possible by use of the most advanced magnetic resonance mass spectrometer, OISM discovery of suitable sample preparation and introduction techniques, and samples from the OISM 5,000 person urine sample bank.

As the years passed, analytical technology advanced. In 2007, donors to the Oregon Institute of Science and Medicine funded a \$1.5 million magnetic resonance mass spectrometer for the OISM laboratory. OISM is supported entirely by private foundations and individual donors. It has never requested or received government taxpayer funds.





This new state-of-the-art mass spectrometer made possible advances in practical metabolic profiling, so OISM scientists resumed research on this subject.

In 2012, OISM received donor funds to pay initial costs for a human urine sample bank which is necessary for this research. About 5,000 people volunteered to provide periodic urine samples and medical information to this bank, which has capacity to hold 200,000 samples at minus 80 °C.

This urine bank is essential. To detect disease before symptoms occur and medical intervention is necessary, we must have samples before overt illness occurs. By cryogenically storing samples from well people, these pre-disease samples and control samples are available for research.

To produce a metabolic profile, a tiny drop of dried urine is laser vaporized, ionized, and then mass analyzed. About 4,000 different urinary chemical constituents with masses below 1,000 atomic mass units are quantitatively measured, of which an estimated one-fourth are human metabolites. The total actual measurement time required is 2 minutes.

The urinary constituents comprise, on average, about 8 adduct and isotopic forms, so about 30,000 substances with different masses are measured and appropriately combined.

Shown in the figure is one of the two mass spectrometers used in this work. The figure below shows part of the urinary mass spectrum of a 93-year-old man. This pictured spectrum is approximately 1/1000th of the total spectrum. Each peak is a unique substance. We currently use about 30 of the shown substances in our calculations.

## **Practical Application**

This discovery of urinary profiles present *before* symptoms of disease and the many profiles discovered earlier for overt illnesses show that profiles will be detectable for essentially all different human biochemical conditions.

With this technology available, it will be possible to optimize human nutrition, lifestyle, and medical techniques.

Essential to this advance is the cost of analysis. In order to reach our goal, these analyses *must* be available to everyone at very low cost, regardless of wealth or current health.

Imagine, for example, a sample kit containing suitable disposable laser-adapted targets of an appropriate fabric on which the user places a drop of urine, allows it to dry, and then mails the target in an ordinary envelope using a 50 cent stamp to a central mass spectrometric laboratory.

Automation places the dried spot of urine in front of the laser for 2 minutes and sends the analysis to the user by mail or confidential Internet, all for a cost of just a few dollars. The user could then rely on an included computerized interpretation, or he could send his data on to a statistical medical evaluation service of his choice. The user can then seek medical or other help if necessary – sending in subsequent samples to measure his progress.

As time passes and he (or she) has submitted samples several times, the machines will be able to customize interpretation of his results to his individual biochemistry, markedly improving the metabolic information.

With the amounts of thousands of substances produced by his metabolism measured regularly and compared to appropriate data bases, he will have definitive quantitative information about his biochemical health.

To optimize biochemical health, minimize disease probability, optimize medical therapy, minimize rate of aging, maximize physical or mental performance, or optimize any aspect of life dependent upon biochemical health – one needs a means of quantitative measurement. Urinary metabolic profiling can provide that measurement. This Oregon Institute of Science and Medicine discovery in predicting heart attacks and breast cancer is just the start. It is the beginning of a major medical advance.



# Living Longer, Better Lives

The figure here summarizes the possibilities of this research. While some people live long lives, most die earlier. They succumb to all sorts of diseases. Moreover, this is not just a question of long life – it is a question of quality of life.

Our goal is to prevent suffering and to increase the quality and length of life. This can be achieved if modern metabolic measurement technology is abundantly available to all people at very low cost. Research at the Oregon Institute of Science and Medicine has this objective.

Excellent physical and emotional health and even the performance of children in school are similarly affected by biochemical health, as measurable in urine metabolites.

Whether the objective is to optimize the health, prosperity and longevity of your children, other loved ones, or yourself, the means of meeting those goals through biochemical research, including metabolic profiling, are similar.

Most importantly, this technology is fast and potentially inexpensive. It could be made available at very low cost – so low that eventually people could have access to it almost as easily as they buy a soft drink from a vending machine.

## **Specific Goals**

Science depends upon quantitative measurement. Only reproducible quantitative experimental measurement can reveal scientific truth – including truth about individual metabolic health. Metabolic profiling has potential to:

1. Measure biochemical health quantitatively. All human performance, including mental acuity, athletic ability, interpersonal relations, work effectiveness, and many other capabilities, depend upon optimum health. This technique can aid in optimizing each person's health.

2. Measure physiological aging. This tells us the chance of a fatal condition arising. If this is quantitatively measured, then guided life style and medical steps can be taken to reduce that chance and extend length of life.

3. Measure the chance of specific illnesses, thus allowing treatment of the probability of illness rather than illness itself – early, when the possibility of success is higher.

4. Detect, diagnose, and monitor the severity and progress of overt disease, thereby facilitating therapeutic therapy by measuring illness quantitatively during treatment.

These goals are shown diagrammatically in the figure. The quantitative patterns found in urine are mathematically converted to the positions of the X marks shown on the axes. Once this is done – conveniently and inexpensively – then the positions of the X marks for each person can be further measured and adjusted to improve his or her life, by means of changes in lifestyle or by medical therapy.

This is analogous to controlling one's personal weight. If no scale were available to measure your weight, it would be difficult to follow your progress. Of course, weight can be seen qualitatively by looking in a mirror. Biochemical health cannot be viewed in this way, and, in both cases, numerical measurements are far more useful.

The keys to this technology are very advanced analytical equipment, measurement methodology so inexpensive that everyone can access it frequently even when in apparent good health, and experimental calibration of the techniques with volunteer urine sample sets large enough to accommodate both rare diseases and biochemical individuality.









#### An Appeal from Art Robinson WE NEED MORE VOLUNTEERS TO PROVIDE OCCASIONAL URINE SAMPLES.

Our current cryogenic bank of urine needs to grow from the current 5,000 volunteers to far more volunteers to provide for less common diseases and individual variations.

We also need to increase our funding. Financial donations, however, are not necessary to become a volunteer.

Current law provides full tax deductions for our donors. It also prohibits our providing analytical health information to any individual. Our volunteers receive only the satisfaction of having helped to further this research.

My scientific and medical colleagues and I, over a period of almost 50 years, have worked to improve human life. At Caltech, UCSD, Stanford, and two independent research institutes we founded, we have always had this goal before us.

This breakthrough in our research – wherein we have analytically discovered, using urine cryogenically stored *before symptoms or medical diagnosis took place*, that individuals needed immediate help to prevent cancer or heart attacks – is a wonderful opportunity to help our fellow Americans.

Please consider participating in this work!

The Oregon Institute of Science and Medicine, 2251 Dick George Road, Cave Junction, OR 97523, is a non-profit 501(c)3 foundation. Our work is supported by donations from private individuals and organizations. Our findings are published in the literature and free for use by everyone.

We need additional volunteers to send periodic urine samples and health information to aid in this research, and we also welcome financial contributions to extend it.