cancer. Most in the community have felt that this would not be possible because tumors are so variant a single vaccine could not be produced. Cancer is too personal. At the genomic level this is true, but we have found that at the RNA processing level this is not the case. Tumors recurrently make the same splicing errors and these errors result in frameshift variants. These frameshift (FS) variants mark the tumor as 'foreign' and open to immunological attack. However, to be effective as a vaccine these antigens must be presented to the immune system (the vaccine) before the tumor starts to develop.

We put in place a process involving 1)bioinformatics screens of tumor cDNA libraries to find FS, 2) screening for the presence of the FS in the RNA of a tumor panel, 3) testing the FS as vaccines in mouse tumor models, and 4) screening human sera from cancer patients for reactivity to the FS. Based on this process we have gathered a collection of FS candidates for a human vaccine. We currently estimate that less than 20 elements will be needed to provide coverage for most cancers.

When we initiated this project ~9 years ago, most in the field doubted such a vaccine could be made. More recently the opinion has shifted to that it may be possible to create such a vaccine but how would it ever be tested for efficacy. Many think the time and cost involved in Phase II/III trials would be insurmountable. However, we have developed a plan based on another invention, immunosignature diagnostics, which may overcome this problem. This technology is based on profiling the antibodies in an individual. It can detect disease, including cancer, early. Our proposal for a Phase II efficacy trial is that potential participants be prescreened for latent cancers. 1000 cancer free people would be entered into the control and vaccine arms of the trial. Individuals would be frequently monitored by immunosignatures for early signs of cancer. The endpoint would be fewer early events in the vaccine versus control arm after 2 years.

Though a clear challenge, it seems feasible that such a vaccine could be developed. Because it could be inexpensive, all the world would benefit from such a vaccine.

S.A. Johnston

A SIMPLE, ONE CHIP DIAGNOSTIC TECHNOLOGY WITH BROAD APPLICATIONS

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In the US 85% of the healthcare costs (~$2.5T/yr) are devoted to taking care of sick people. To change this situation, healthcare must convert from post-symptomatic treatment to prevention and early detection/treatment of disease. We have invented a technology that may facilitate early detection of any disease.

Immunosignaturing diagnostic technology is premised on the idea that the antibody profile of an individual at a given time is a reflection of their health status and that people with common illnesses will present similar profiles. With ~109 different antibodies in a person at a given time the challenge is to splay out enough of them to diagnose. We found that we can do this effectively with chips with ~3×105 random sequence peptides on them. The peptides are synthesized using computer chip lithography technology so it is scalable.

In the current practice a drop of blood is sent through the standard mail on a filter paper. The drop is diluted ~5000 fold in buffer and applied to the chip. Unbound material is washed off and the antibodies detected with a secondary antibody. It is a very simple, robust process. No processing of the sample is required. The signature algorithm for each disease is produced by comparing a sufficient number of affected and not affected people. The same chip is used for every type of disease diagnosis.

We have applied this technology to distinguish cancers, Alzheimer's disease, diabetes and numerous infectious diseases. The technology has also been used for early detection of disease and evaluation of vaccine candidates.

Our vision is that all people will regularly send in a drop of blood to be monitored for any indication of disease. This will be done for little cost and be highly specific. Eventually the system could be in the home. In this way we could transition to a truly presymptomatic health system.

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BRAF-ОНКОГЕН ПРИ НОВООБРАЗОВАНИЯХ ЩИТОВИДНОЙ ЖЕЛЕЗЫ

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Папиллярный рак щитовидной железы (ПРЩЖ) составляет от 65 до 85% всех злокачественных опухолей этого органа. Новообразование характеризуется благоприятным прогнозом для жизни. Однако от 10 до 15% ПРЩЖ отличаются агрессивным поведением, дают ранние метастазы и имеют высокий показатель смертности. Соматическая мутация в гене *BRAFV600E* считается наиболее распространенным молекулярным дефектом при спорадическом папиллярном раке (39—83%), характерна для более агрессивного течения заболевания и определяется уже при I стадии.

Нами была выполнена работа по определению BRAF-мутаций при новообразованиях щитовидной железы. Всего обследован 131 человек с узловыми образованиями щитовидной железы, выявленными при ультразвуковом исследовании. Женщин было 123, мужчин – 8, средний возраст обследованных составил 51,9 года. Всем пациентам выполнена тонкоигольная биопсия под контролем УЗИ. Все цитологические мазки окрашивались по методике Папаниколау. Исследования по выявлению мутаций гена *BRAF* выполнялись в отделе молекулярной медицины Института радиационно-индуцированных заболеваний Университета Нагасаки, Япония.

Были получены следующие данные: папиллярные карциномы составили 77 (56,2%) случаев, доброкачественные опухоли — 18 (13,1%), фолликулярный неоплазм – 15 (10,9%), подозрение на рак – 15 (10,9%), фолликулярная карцинома – 8 (5,8%), низкодифференцированная карцинома – 2 (1,5%), злокачественная лимфома – 1 (0,72%). Из 77 пациентов с ПРЩЖ мутации *BRAF*-гена обнаружены в 19 (24,6%) случаях. При